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IN SOMNO SECURITAS

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rescribing information
dications and dosage: Systemic
ndidiasis: 400mg on the first day
llowed by 200-400mg once daily.
ryptococcosis, including meningitis:
0mg on the first day followed by
0-400mg once daily.
aintenance therapy to prevent
lapse of cryptococcal meningitis in
tients with AIDS: at least 100mg
ily. Oropharyngeal candidiasis:
-100mg once daily for 7-14 days
longer in immunocompromised
tients. Other mucosal candidal
fections: 50-100mg once daily for
-30 days. Vaginal candidiasis:
ngle 150mg dose. Use in the elderly
s above except for those renally
paired - see data sheet.
se in children - not recommended.
dministration: Diflucan may be
dministered either orally or by
travenous infusion at a rate of
proximately 5-10ml/min. The
sages for the two routes are
uivalent. *Contra-indications*:
ypersensitivity to fluconazole
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arnings: Lactation: Not
commended. Renal impairment:
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lendar pack of 7, £66.42 (PL
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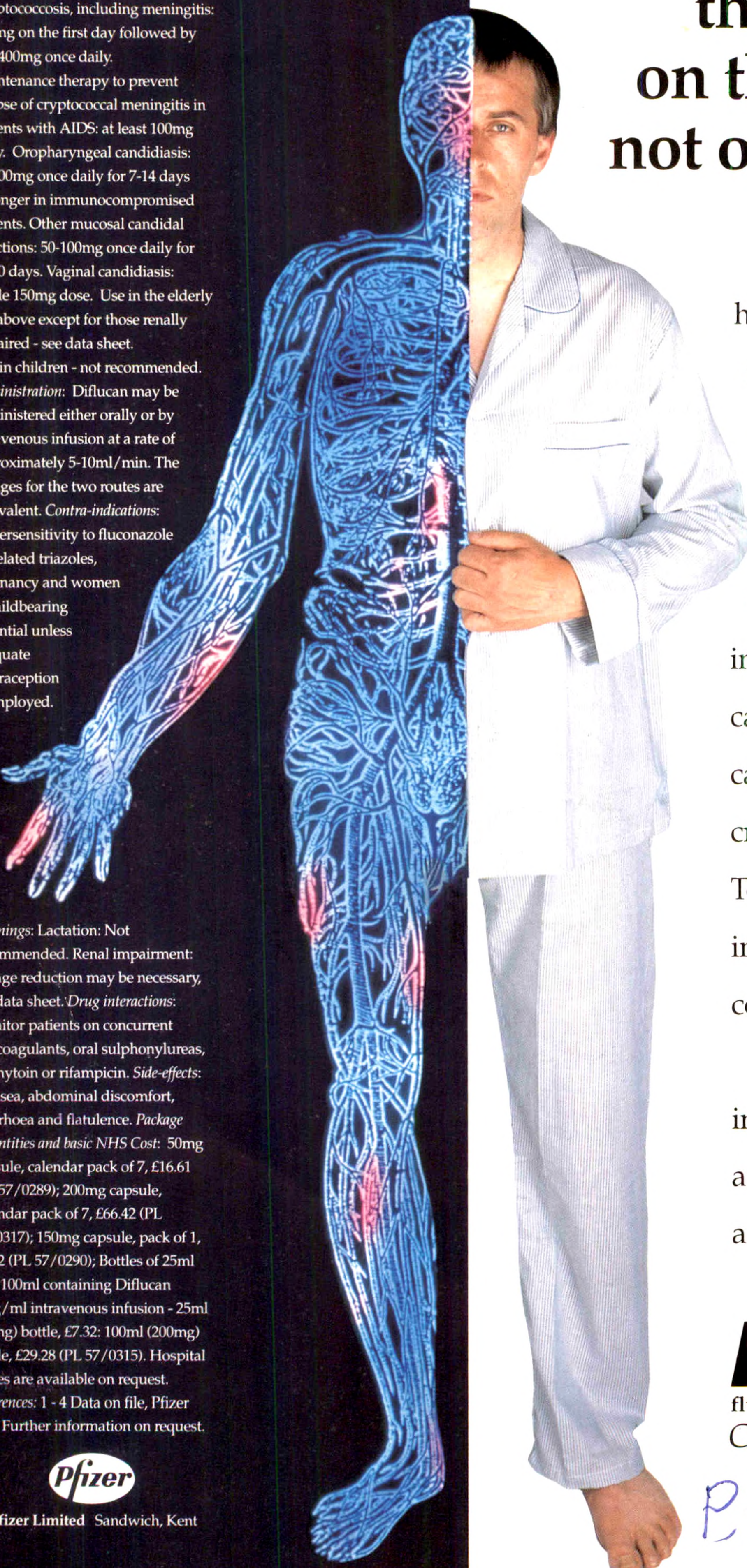

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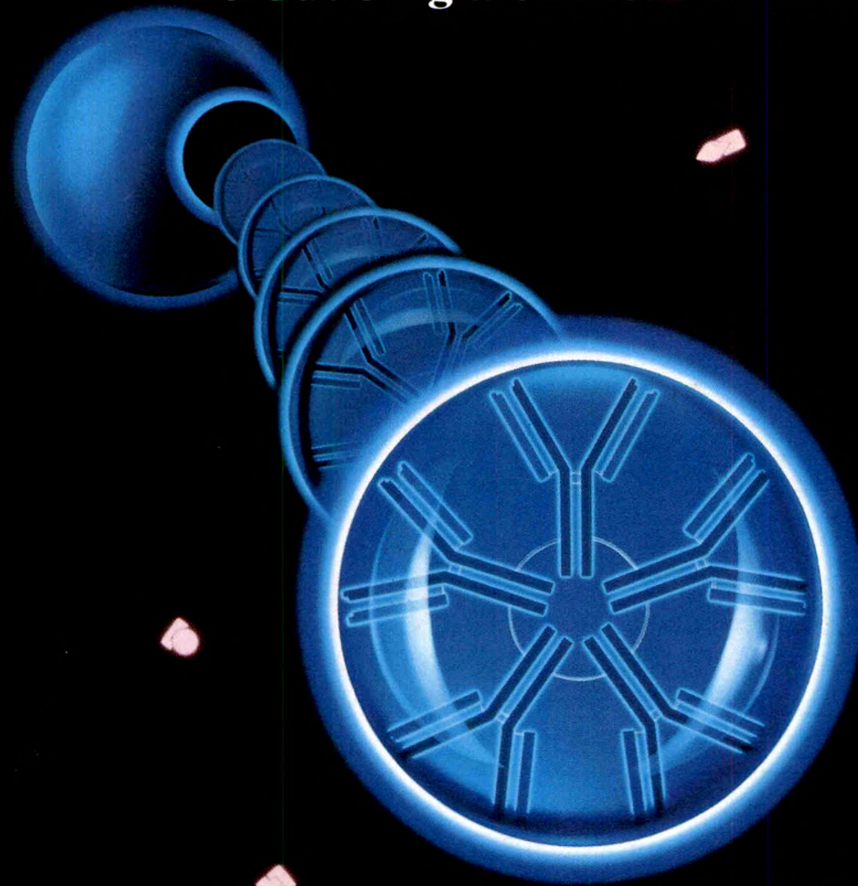

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Life-saving therapy for Gram-negative sepsis and septic shock

ABBREVIATED PRESCRIBING INFORMATION

PRESENTATION Centoxin is a solution for intravenous infusion after dilution with normal saline. Each vial contains: HA-1A 100 mg/20 ml

USES Centoxin is indicated for the treatment of patients with the sepsis syndrome and a presumptive diagnosis of Gram-negative bacteraemia, especially those with septic shock. Centoxin therapy should be given in hospital, along with the appropriate antibiotics and supportive therapy, as soon as Gram-negative sepsis is clinically suspected. Centoxin should be given once and is not intended for repeated use.

DOSAGE AND ADMINISTRATION The recommended dose of Centoxin is a single 100 mg intravenous infusion. Centoxin should be administered intravenously over a period of 15 to 30 minutes in a total volume of 70 mL after dilution with normal saline for injection. In patients studied to date, it has not been necessary to adjust the dosage for renal or hepatic function.

CONTRA-INDICATIONS, WARNINGS ETC. **Contra-indications** Centoxin should not be used in patients whose primary injury involves burns, since no studies have been done in those patients. Centoxin should not be used in patients with known hypersensitivity to murine proteins. Centoxin should not be used in patients with previous exposure to HA-1A. **Undesirable Effects** No serious or life-threatening adverse reactions attributable to Centoxin were reported among the more than 300 patients who received the product in clinical trials, including more than 45 patients who received 200 or 300 mg of HA-1A as a single dose. Transient flushing, localized urticaria and hypotension have been reported rarely (<1%) in patients receiving Centoxin. Human antibodies against Centoxin have not been detected. **Special Precautions** *In vitro* and *in vivo* mutagenicity studies have not demonstrated any mutagenic effect. Studies have not been performed to evaluate the carcinogenic potential or effects on fertility in male or female animals. The use of Centoxin in children has not been extensively studied. Centoxin has been administered to a small group of children (ages 10 months to 13 years), the majority of whom had fulminant meningococcaemia with shock and purpura. The dose administered was up to 6 mg/kg to a maximal dose of 100 mg. Centoxin was well tolerated by all patients. The efficacy of Centoxin in adults and children with meningococcal septicaemia has not been established and therefore the use of Centoxin in meningococcal septicaemia cannot be recommended. Centoxin contains a murine J chain, which suggests that anti-HA-1A

CENTOXIN: The first human monoclonal antibody specifically directed against endotoxin

Centoxin (HA-1A) is a human monoclonal IgM antibody targeted against endotoxin – the substance largely responsible for multiple organ failure and death associated with Gram-negative sepsis and septic shock. Centoxin neutralizes the lethal effects of endotoxin and helps save the lives of septic patients.

Early and sustained reductions in mortality in Gram-negative sepsis and septic shock

In a multicentre, double-blind, placebo-controlled trial, Centoxin was administered to septic patients with presumptive Gram-negative bacteraemia, including those with septic shock. Clinical results demonstrate significant early and sustained reductions in mortality in septic patients with Gram-negative bacteraemia, especially those with septic shock.[1]

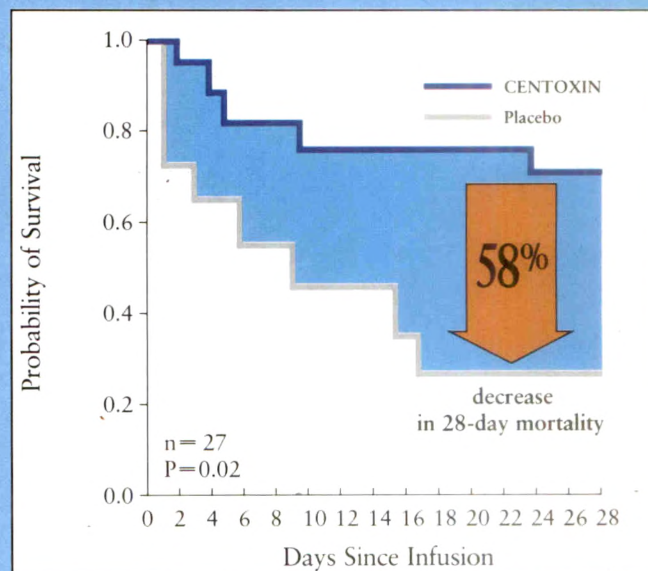
Reduction in 28-day mortality[1]

	Mortality			
Population	Placebo*	Centoxin	% Reduction	*P* Value
Gram-Negative Bacteraemia (N=200)	49% (45/92)	30% (32/105)	39%	0.014
Gram-Negative Bacteraemia with Shock (N=102)	57% (27/47)	33% (18/54)	42%	0.017

*Three placebo-group patients (one with shock) were discharged from the hospital and lost to follow-up before day 28.

58% decrease in mortality in endotoxaemic patients[2]

Centoxin decreased mortality in endotoxaemic patients – patients in whom a human anti-endotoxin monoclonal antibody should work best.



Centoxin:

- Effective in significantly reducing mortality in both severely ill and less severely ill patients with:
  - shock and without shock[1]
  - high APACHE II scores (>25) and low APACHE II scores (≤25)[1]
- Safe and nonimmunogenic in clinical studies conducted to date[1,3]
- Administered in a single fixed dose regardless of disease severity, renal and hepatic function

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(HA-1A)

Saving lives in Gram-negative sepsis and septic shock

antibody formation is a possibility. Nevertheless, in clinical trials, anti-HA-1A antibodies were not detected (with a radioimmunoassay) in blood samples taken from patients up to 35 days after administration of a single dose of Centoxin. The immunogenic risk of repeated administration of Centoxin has not been extensively investigated. **Use During Pregnancy and Lactation** There has been no experience to date with the use of Centoxin in pregnant patients, and animal reproduction studies have not been conducted. Therefore, Centoxin should be used in pregnant patients only when, in the judgement of the physician, anticipated benefits outweigh the potential risks. It is not known if Centoxin is excreted in human milk. **Interaction with Other Medicaments and Other Forms of Interaction** There have been no reports of interactions between Centoxin and other drugs used concomitantly in the treatment of Gram-negative sepsis. **Overdose** The maximum amount of Centoxin that can safely be administered has not been determined. However, single doses as high as 300 mg of Centoxin have been safely administered to adults, and doses of 6 mg/kg up to a maximum of 100 mg to children from 10 months to 13 years of age. **Effects on Ability to Drive and Use Machines** HA-1A is pharmacologically inert and can therefore not be expected to affect the ability to drive and use machines. It is, in any case, administered only to hospitalized, seriously ill patients.

LEGAL CATEGORY POM.
PACKAGE QUANTITIES Centoxin is available as a package containing 1 single dose 20 ml vial. **Product licence number** 8563/0010 **Basic NHS cost** £2,200. **Date of preparation** May 1991. For further information refer to data sheet or contact: Centocor Medical Services, Centocor B.V., Einsteinweg 101, 2333 CB Leiden, The Netherlands Tel. 0800-898458 A 2001

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Anaesthesia, 1991, Volume 46, pages 613–614

Editorial

Anticoagulant drugs and central nerve blockade

Traditional teaching has always maintained that the major regional anaesthetic techniques are contraindicated in the presence of disorders of coagulation. When these methods were little used this proscription simply reinforced the then current practice, but the last two decades have seen a major increase in the employment of central nerve block. This increased frequency of use started in obstetrics, is spreading progressively into other areas of anaesthetic practice and has made concern about the risks of therapy with drugs that affect coagulation more practically relevant. Such is the concern that it may lead to patients being denied regional anaesthesia and this issue of *Anaesthesia* includes a survey of Danish practice which has found that low dose heparin therapy is considered a contraindication to epidural block in 38% of departments.[1]

This concern has been heightened by a number of other factors besides the wider use of heparin in the prophylaxis of thrombo-embolic complications of surgery. First there is greater knowledge of the subtler effects of certain drugs on the coagulation process, notably the influence of the nonsteroidal anti-inflammatory analgesic drugs on platelet function. Secondly, the use, availability of, and indications for, such drugs have all increased; the use of low dose aspirin in the prevention of thrombotic sequelae of arterial disease and in the treatment of pre-eclampsia are particularly relevant. Thirdly, agents which actively dissolve thrombus, such as streptokinase, are being used more widely in the management of peripheral vascular disease. As a result, patients receiving drugs which interfere with coagulation are not only more likely to be encountered, but they are also often the very ones for whom a central block has most to offer.

In attempting to rationalise this dilemma, it is necessary to start by delineating exactly what we are worried about. Insertion of a needle or catheter into the vertebral canal will occasionally damage a blood vessel; the frequency is as high as 18% in the obstetric population.[2] If coagulation is abnormal the bleeding may not stop and lead to the accumulation of a haematoma, usually in the epidural, rather than the subarachnoid, space. This haematoma is assumed to compress the spinal cord or the cauda equina and result in paraplegia, which may be permanent unless the haematoma is evacuated promptly. Possible warning signs are intense but localised back pain and the signs of progressive spinal cord compression.

A number of difficulties exist in assessing the risk after central nerve blockade. First, spinal haematoma is a very rare condition, but does occur spontaneously in patients who have neither a disorder of coagulation nor history of instrumentation of the vertebral canal.[3] Secondly, it has been described in both the puerperium[4] and postoperative period[5] in patients who have *not* received regional techniques. Clearly then, the insertion of a needle and development of a haematoma may not necessarily be causally related. Because the condition is rare, a huge series would be needed to gauge the risk after central block, whether coagulation is normal or not.

Such considerations require that a very thorough search is made for other factors (such as injection errors) in each case, but they do not mean that anaesthetists can ignore the problem. In a very extensive review of the literature, Sage[6] found that the great majority of spinal haematomata occurring after central nerve block were in patients with coagulation disorders. This leads some to eschew these methods altogether, but this is somewhat illogical given our lack of knowledge and the rarity of the condition. The alternative strategy is to develop clear policies on the use of regional anaesthesia in these situations, bearing in mind that there are no absolute indications or contra-indications for any technique and that all decisions involve balancing relative risks. The strategies devised must, however, err on the side of safety until better data are available on the true incidence of the condition.

If a haematoma is to develop, it is obvious that there must be damaged vessels as well as a disorder of coagulation. From basic principles it would seem that the more blood vessels are damaged, the more likely is a haematoma, although there is little evidence to support this. Difficulty in identifying the epidural or subarachnoid space is not a regular feature of case reports. Secondly, there does not seem to be any difference in incidence between continuous epidural and 'single shot' subarachnoid block, although the former does seem inherently more 'traumatic'. Clearly though, it behoves all practitioners of regional anaesthesia to try and minimise the amount of vessel damage that occurs and to employ Bromage's 'gossamer' touch.[7] The final corollary of this consideration is that the experience and expertise of the anaesthetist who will perform the block is vital. What may be a reasonable decision for an experienced, senior clinician might be a very unwise one for the beginner.

Against this background the following advice is offered for various clinical situations.

Pre-operative anticoagualant or thrombolytic therapy. The majority of published reports of spinal haematoma after epidural injection have been in patients with bleeding diatheses. Thus full anticoagulation with warfarin or heparin, and thrombolytic therapy with streptokinase, should contraindicate central nerve block if other means of anaesthesia or analgesia are available. However, it is unlikely that surgery or labour will proceed with full anticoagulation and there is no reason why the timing of the withdrawal of drug therapy, checked by the appropriate laboratory investigation, cannot be influenced by the choice of anaesthetic.

Low dose heparin therapy. A much commoner problem is the use of subcutaneous heparin in the prophylaxis of thrombo-embolic disease. It is argued that the concomitant use of central nerve block is safe,[1] but some patients develop significant systemic concentrations of

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heparin within 2 hours of administration.[8] Thus it would seem wise to avoid instituting a block within 4–6 hours of its administration if possible. A clear policy should be established with the surgeons, many of whom will accept that the block gives more than sufficient peri-operative protection against deep vein thrombosis. Thus the pre-operative dose may be omitted or, alternatively, may be given in the anaesthetic room *after* the block has been instituted.

Aspirin therapy. Much of the current concern about coagulation disorders and regional anaesthesia is related to the use of low-dose aspirin in the control of pre-eclampsia. Aspirin, by its effects on platelet aggregation, has effects on the coagulation process that may last for 7–10 days,[9] yet epidural block may be positively indicated in these patients. This is a new clinical situation and it is difficult to give categorical advice, but it is important to remember that the changes in platelet function that do occur are very subtle and require sophisticated tests for their demonstration.

It has been argued that the clinically relevant test is the bleeding time, that the kit for its measurement should be available in all areas where epidural block is used and that 10 minutes should be considered the upper limit of normal.[10] However, this is a test that requires close attention to detail and a very standard technique to produce reliable results.[11] There is a need for large series of measurements to be performed to establish the variability in results produced when the test is used routinely by clinicians, and also to define the normal range in late pregnancy. Until the results of such studies are available the risks of false negative and positive results leading to incorrect clinical decisions are great.[9]

Peroperative anticoagulant therapy. Central nerve blocks have been used in large series of patients undergoing peripheral vascular surgery during which heparin was administered.[12] The heparin is rarely given within an hour of institution of the block so that any bleeding caused at that time has every opportunity to stop. Some practitioners consider that bleeding at the time of catheter insertion is an indication for postponing the operation, but we know of no evidence that supports such a disruptive policy. Some, particularly those who use epidural block for cardiac surgery when very large doses of heparin are given, prefer to insert the catheter on the day before surgery.

Postoperative anticoagulant therapy. If patients are to receive these drugs after surgery or delivery, it is sensible to give some thought to the timing of catheter removal. If warfarin is to be given the catheter should be removed well before the drug becomes effective, but heparin infusion may be commenced as soon as a vascular procedure is complete. The safest course is to stop the heparin for 1–2 hours before catheter removal, the time for this being chosen in consultation with the surgeon. Finally, if the patient continues to receive subcutaneous heparin the catheter should be removed about an hour before a dose is due.

Conclusion

The use of drugs that influence coagulation must be a concern to anaesthetists who use regional methods, although it is essential to maintain a sense of proportion and to make a balanced assessment of the particular risks. It is a source of reassurance to many that Odoom and Sih have documented the safe administration of epidurals to 1000 patients receiving anticoagulant drugs, albeit with very strict guidelines.[13] However, even this number is small given the infrequency with which spinal haematomata occur and we must recognise that we know neither the numerator nor the denominator. Is there a place for a national registry of the condition as a basis for future risk assessment?

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Editorial notices

Manuscripts must be submitted in accordance with the internationally recognised *Uniform requirements for manuscripts submitted to biochemical journals* (*British Medical Journal* 1979: **1**: 432 5). Details will be found in the Notice to Contributors to *Anaesthesia* at the end of this issue.

Anaesthesia, 1991, Volume 46, pages 615–622

Induction and recovery characteristics of desflurane in day case patients: A comparison with propofol

S. R. WRIGLEY, J. E. FAIRFIELD, R. M. JONES AND A. E. BLACK

Summary

Desflurane is an ether halogenated exclusively with fluorine. It has a blood/gas partition coefficient of 0.42 (cf. isoflurane 1.40 and nitrous oxide 0.46). This characteristic suggests that it should provide both a fast induction of anaesthesia and a rapid recovery from anaesthesia. To assess this, 60 patients were entered into a study and allocated at random to one of four groups receiving either desflurane or propofol for induction and maintenance of anaesthesia. Desflurane caused loss of consciousness in approximately 2 minutes during gaseous inductions. The psychomotor scores in the patients who received propofol for induction and maintenance of anaesthesia were significantly worse compared with those who were given desflurane for either induction and maintenance or for maintenance only. There was also a tendency for other recovery parameters to be faster in the patients receiving desflurane although this did not reach statistical significance. This suggests that desflurane would be a suitable agent for day case anaesthesia providing for a rapid recovery.

Key words

Anaesthetics, volatile; desflurane.
Anaesthetics, intravenous; propofol.
Surgery; day case.

Desflurane (difluoromethyl 1-fluoro 2,2,2,-trifluoro ethyl ether) is an ether halogenated exclusively with fluorine. The chemical structure is similar to isoflurane; the chlorine on the alpha ethyl carbon is substituted with fluorine. Desflurane has a blood/gas partition coefficient of 0.42[1] (cf. isoflurane 1.40 and nitrous oxide 0.46) and has a not unpleasant odour.[2] It has been demonstrated to have no measurable effects on renal or hepatic function,[3,4] to have good cardiovascular stability[2,5] and to provide a rapid recovery from anaesthesia in animals.[6] These characteristics suggest that it should provide a rapid induction and fast recovery from anaesthesia and would be a suitable agent for anaesthesia during day case surgery.

We studied the induction, maintenance and recovery characteristics using desflurane, in comparison with propofol, in patients undergoing peripheral orthopaedic surgery on a day case basis.

Method

The study was approved by the Hospital Ethics Committee and a Clinical Trials Exemption Certificate for desflurane obtained. All patients gave written informed consent to participate in the trial.

Patients

Sixty patients between the ages of 18 and 70 years, of ASA 1 or 2, who presented for peripheral orthopaedic operations to be performed on a day case basis were entered into the study and allocated at random to one of four groups (Table 1).

All patients were seen by one of the investigators, a medical history was taken and clinical examination performed. Patients who had received an anaesthetic within

Table 1. Methods of anaesthesia induction and maintenance.

Group	Induction	Maintenance
1	Propofol	Desflurane/N_2O/O_2
2	Propofol	Propofol/N_2O/O_2
3	Desflurane/N_2O/O_2	Desflurane/N_2O/O_2
4	Desflurane/O_2	Desflurane/O_2

S.R. Wrigley, FCAnaes, Research Registrar, J.E. Fairfield, FCAnaes, Lecturer, R.M. Jones, MD, FCAnaes, Professor, A.E. Black, FCAnaes, Senior Registrar, Departments of Anaesthetics, St Mary's and Guy's Hospitals, London.
An abstract of this work was presented at the Anaesthetic Research Society, Edinburgh on 10 November 1990.
This study was supported in part by a grant from Anaquest Inc. (New Jersey), a division of the British Oxygen Company.
Correspondence should be addressed to Professor R.M. Jones, Department of Anaesthetics, St Mary's Hospital, Paddington, London W2 1NY.
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the previous 7 days were not studied, as were females of child bearing potential, and those with a personal or family history of malignant hyperthermia, an unusual response to previous anaesthetics, a history of lung disease that would affect the uptake or distribution of an inhalational agent, or chronic exposure to any drug which would affect anaesthetic requirements e.g. narcotic analgesics, tranquillisers, alcohol or antidepressants. Following this the nature of the study was explained and written consent obtained. Baseline psychomotor tests were then completed by the patient.

Psychomotor tests

The psychomotor tests used were 'p' deletion and digit symbol modalities test (DSM). In the p-deletion test the patient was presented with a sheet of 58 lines containing closely packed random letters and asked to delete as many letter ps as possible without omission, reading from left to right in a 3-minute period. The test was scored by counting the number of lines completed and the number of errors made (one error for each p missed and two for deleting an incorrect letter). The test provides a measure of vigilance i.e. the ability to sustain attention.

The DSM test consists of a sheet of paper, at the top of which appears a key, numbers 1–9, each number being ascribed a different symbol. Beneath the key are eight rows of 25 randomly distributed numbers without their corresponding symbol. The patient was asked to substitute as many symbols as possible in a 2-minute period starting with the first row and working from left to right. The test was scored by counting the number of correct symbols inserted. The test assesses an individual's ability at sustained, focused concentration and directed visuomotor scanning.

Anaesthesia—Induction

All patients were unpremedicated. Intravenous access was established and an infusion of compound sodium lactate solution given (0.5 ml/kg for every hour that the patient had been starved) before surgery. All patients were preoxygenated with 100% oxygen for 2 minutes, and received tubocurarine 3 mg/70 kg. The patients allocated to groups 1 or 2 were given fentanyl up to 2 μg/kg and anaesthesia was then induced with propofol 2.5 mg/kg. In patients allocated to group 3, anaesthesia was induced with desflurane and nitrous oxide in oxygen (40%) followed by fentanyl up to 2 μg/kg. In group 4 anaesthesia was induced with desflurane in oxygen followed by fentanyl up to 2 μg/kg. The initial inspired concentration of desflurane was 3.0–3.6% and increased by 3% increments every 2–3 breaths until the patient lost consciousness (up to a maximum inspired concentration of 12%). All patients received suxamethonium 1–1.5 mg/kg to facilitate tracheal intubation.

Anaesthesia—Maintenance

Anaesthesia was maintained in groups 1 and 3 with desflurane 6% and nitrous oxide in oxygen (40%), in group 4 with desflurane 6% in oxygen and in group 2 with a propofol infusion (9 mg/kg/hour for 15 minutes and then 6 mg/kg/hour) supplemented by nitrous oxide in oxygen (40%). The anaesthetic was delivered by a modified Ohio DM 5000 anaesthesia machine with an electrically heated, temperature-controlled vaporizer, via a circle system with soda lime carbon dioxide absorber using an Ohmeda 7000 ventilator. The end-tidal desflurane concentration was measured with a Datex Multigas anaesthesia monitor modified for desflurane. The lungs of all patients were ventilated to normocapnia, and vecuronium 0.05 mg/kg was given as considered necessary. The patients' systolic and diastolic arterial pressures, heart rate, oxygen saturation, temperature, neuromuscular function, end-tidal carbon dioxide, and where appropriate end-tidal desflurane concentrations were monitored. All these data were recorded before induction of anaesthesia, at 2-minute intervals from induction to incision, every minute for 5 minutes from incision and then every 15 minutes until the end of surgery. At the discretion of the responsible anaesthetist the percentage of desflurane was adjusted or extra doses of propofol administered either as a bolus (10–20 mg) or by altering the infusion regimen (up to 12 mg/kg/hour).

Recovery

At the end of anaesthesia residual neuromuscular paralysis was antagonised with neostigmine 0.05 mg/kg given with glycopyrronium 8 μg/kg as necessary, and 100% oxygen administered. Following tracheal extubation the patient was transferred to the recovery room receiving supplemental oxygen via a facemask. In the recovery room indirect arterial blood pressure, heart rate and oxygen saturation were measured at 15 minute intervals for one hour. Supplemental oxygen was maintained until the patient no longer tolerated the facemask. Analgesic and antiemetic medication was given as necessary.

Assessment

The quality of induction was assessed by noting the incidence of apnoea, breath-holding, laryngospasm, bronchospasm, coughing, secretions, excitation, spontaneous and purposeful movement. The end-tidal concentration of desflurane causing loss of consciousness, as judged by the loss of the eyelash reflex and loss of response to verbal commands, was recorded together with the time taken from the start of induction.

Recovery from anaesthesia was assessed by a blinded observer. The time taken from the end of anaesthesia for the patient to open his/her eyes, and to respond to the commands 'squeeze my fingers', 'tell me your name', and

Table 2. Criteria used to score pain and sedation.

Verbal pain score	
1	None
2	Mild
3	Moderate
4	Severe
5	Excruciating
Sedation score	
1	Asleep and not arousable
2	Asleep but difficult to arouse
3	Asleep but easily arousable
4	Awake and calm
5	Awake and hyperactive

Table 3. Laboratory investigations performed before and after operation.

Biochemistry	Haematology	Urinalysis
Sodium	Red cell count	Specific gravity
Potassium	Total haemoglobin	pH
Chloride	Haematocrit	Glucose
Glucose	Platelets	Protein
Urea	Total white count	Casts
Creatinine	Neutrophils	Crystals
Total bilirubin	Lymphocytes	White cells
Aspartate transaminase	Monocytes	Red cells
Alanine transaminase	Basophils	Bacteria
Alkaline phosphatase	Prothrombin time	
Bicarbonate		
Albumin		
Calcium		

'tell me your date of birth' were noted. Psychomotor tests of p deletion and DSM were completed by the patient at 30-minute intervals for 2 hours after anaesthesia. The times from the end of anaesthesia for the patient to sit, stand, walk, tolerate oral fluids, and to be orientated in time and place were recorded.

Postoperative pain was evaluated at 30-minute intervals for 2 hours with a verbal pain score and a 10 cm visual analogue scale, together with a sedation scale (Table 2). Any side effects or adverse events such as nausea and vomiting were noted. Where possible all patients were contacted the following day and asked about intra-operative recall and any adverse events.

In all patients blood and urine samples were obtained pre- and postoperatively for the tests as shown in Table 3.

The results were analysed using the Chi-squared (with Yates' correction) t-test, confidence intervals and ANOVA where appropriate. Statistical significance was assumed at $p < 0.05$.

Results

Three patients, one in group 3 and two in group 4, have been omitted from analysis since they did not tolerate a gaseous induction. The four groups were comparable for demographic data, as shown in Table 4.

Induction characteristics

The times for loss of consciousness to occur, as judged by the loss of the eyelash reflex and response to verbal commands for groups 3 and 4 are shown in Table 5.

Induction was faster in group 3, but not significantly so, and the end-tidal concentration of desflurane at which this occurred was lower. Gaseous induction was sometimes associated with a brief period of excitation with spontaneous and purposeful movement, which was more frequent in group 4 than group 3, although there was no recollection of this by the patients. There were six patients in group 3 and 10 in group 4 in whom coughing occurred. This was associated with breath-holding in seven of the patients in group 4 and one in group 3. One patient in group 3 vomited at induction; however, there was no evidence of aspiration, surgery continued uneventfully, there were no postoperative sequelae, and the patient had no recollection of the event. The overall induction sequence in groups 3 and 4 was slightly longer than in groups 1 and 2 (Table 4).

Whenever an excitation phase occurred in patients in groups 3 and 4 this was accompanied by an increase in the systolic and diastolic blood pressures with an associated increase in heart rate (Figs 1–3).

Maintenance

The type and duration of surgery (Table 4) was similar in all four groups. There were three patients in both groups 1 and 3, and one in group 4 who required atropine for an episode of bradycardia. In addition there were five patients in group 1 and four in group 3 who had a brief self-limiting episode of a nodal rhythm.

Nine patients in group 2 required further neuromuscular relaxation to facilitate ventilation compared with two in

Table 5. Length of time and end-tidal desflurane concentration causing loss of consciousness for gaseous inductions. Values expressed as mean (SD).

	Group 3	Group 4
Time; minutes	2.0 (1.1)	2.6 (1.1)
Desflurane concentration; %	5.9 (2.0)	6.5 (2.0)

Table 4. Demographic data of patients. Values expressed as mean (SD) or whole numbers.

	Group 1	Group 2	Group 3	Group 4
Age; years	36.2 (11.7)	37.2 (14.0)	39.2 (11.0)	43.5 (15.6)
Weight; kg	74.4 (10.6)	73.0 (14.4)	75.6 (15.9)	72.7 (14.0)
Height; cm	170.4 (8.3)	176.8 (6.2)	172.7 (10.5)	170.4 (8.5)
Sex; M:F	12:3	14:1	11:3	9:4
ASA; 1:2	12:3	15:0	12:2	11:2
Race; C:B	14:1	13:2	14:0	13:0
Induction–Incision time; minutes	12.8 (4.6)	11.3 (3.4)	13.9 (3.0)	15.0 (2.3)
Operation time; minutes	35.5 (22.1)	27.3 (20.7)	25.5 (14.1)	29.0 (15.2)

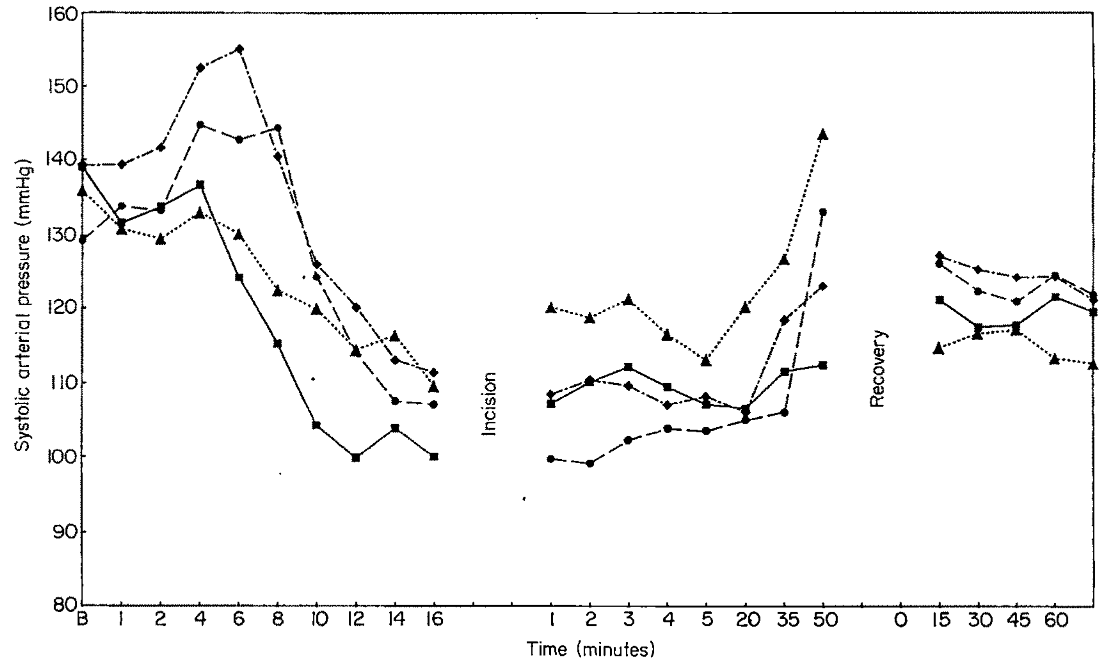

Fig. 1. Mean systolic arterial pressure. -■-, group 1; ···▲···, group 2; --●--, group 3; ---◆---, group 4.

group 1 and one in both groups 3 and 4 (group 1, $p < 0.05$; groups 3 and 4, $p < 0.02$ cf.; group 2, Chi-squared with Yates' correction). The end-tidal concentration of desflurane at the end of anaesthesia in groups 1, 3 and 4 were similar (mean (SD in %): 6.4 (1.1): 6.2 (1.8): 6.1 (2.2) respectively). The patients in group 2 received a mean infusion rate of propofol of 7.68 mg/kg/hour (SD 0.73, range 6.8–9 mg/kg/hour, median 7.5 mg/kg/hour).

Recovery

The mean and median times taken for orientation to occur and for the patients to open their eyes and respond to the commands 'squeeze my fingers', 'tell me your name' and 'tell me your date of birth' were shorter in group 4, but this did not reach statistical significance. The mean times in group 2 were longer, although the median times were comparable with groups 1 and 3. There was no difference between the groups in the time taken to sit, stand and walk, and to take oral fluids (Table 6).

Seven patients (three in group 1, one in groups 2 and 3, and two in group 4) required admission to the ward as the surgery was more extensive than originally anticipated; they were unable to mobilise early and were not included in the analysis for the time taken to stand and walk.

The incidence of nausea and vomiting in patients who

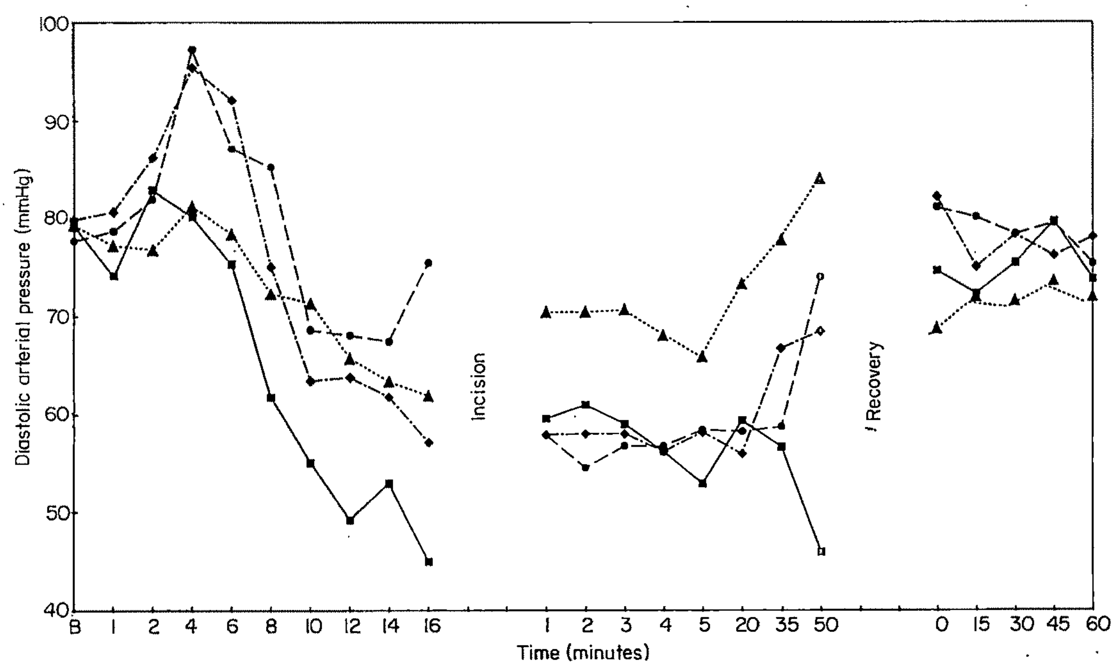

Fig. 2. Mean diastolic arterial pressure. -■-, group 1; ···▲···, group 2; --●--, group 3; ---◆---, group 4.

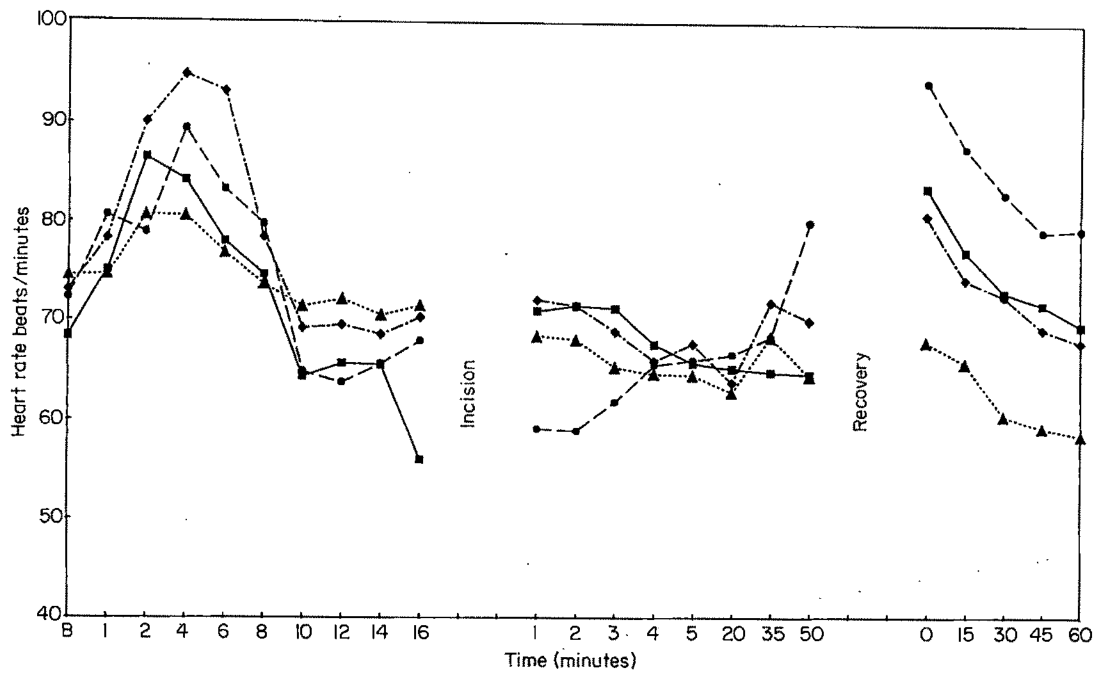

Fig. 3. Mean heart rate. -■-, group 1; ···▲···, group 2; --●--, group 3; ---◆---, group 4.

received desflurane was greater than in the patients who did not (Table 7).

The change in psychomotor scores from baseline (pre-operative minus postoperative score) and the proportional change from baseline (ratio pre-operative minus postoperative: pre-operative score) were analysed, having first confirmed that the data were normally distributed. The psychomotor scores for the DSM and the p deletion, with respect to the lines completed at 30 minutes, was significantly worse in group 2 (Fig. 4). The scores in group 2 for these tests remained significantly different from the baseline for 2 hours postoperatively, whilst those in groups 1, 3 and 4 did not (Figs 5 and 6). There was no difference either between the groups or in their change from baseline with the p-deletion test for errors or errors per line scored. All patients were able to complete the tests at 30 minutes after operation.

The visual analogue pain scores were comparable at each time interval for all groups and tended to decrease with time (Table 8). Between six to eight patients in each group required analgesia which was initially given in the form of oral medication. Two patients in both groups 2 and 4 required parenteral opioids during the 2 hour postoperative observation period. The majority of the time the patients were awake and calm.

Only one patient could not be contacted the following

Table 6. Times from end of anaesthesia for these to occur. Values expressed in minutes as mean: median (SD).

	Group 1	Group 2	Group 3	Group 4
Open eyes	8.2:8 (3.5)	9.4:8 (4.9)	8.0:9 (3.2)	6.2:6 (3.0)
Squeeze my fingers	9.4:10 (4.4)	10.0:9 (4.8)	8.9:9 (3.2)	6.5:6 (3.5)
Name	10.1:9 (4.0)	11.0:9 (5.4)	9.8:9 (3.7)	7.1:6 (3.3)
Date of birth	10.2:9 (4.0)	11.2:10 (5.4)	10.0:9 (3.6)	7.8:7 (3.4)
Orientated	13.6:13 (5.0)	12.9:12 (4.9)	11.1:11 (4.5)	11.1:8 (7.1)
Sitting	38:38 (16)	34:26 (21)	26:23 (6)	32:33 (11)
Stand/walk	118:111 (35)	107:108 (27)	103:106 (14)	89:82 (20)
Taking fluids	49:53 (25)	55:50 (31)	37:26 (24)	36:31 (18)

Table 7. Postoperative nausea and vomiting. Total number of patients.

Event	Group 1	Group 2	Group 3	Group 4
Nausea	7	1	6	3
Vomiting	2	0	4	0

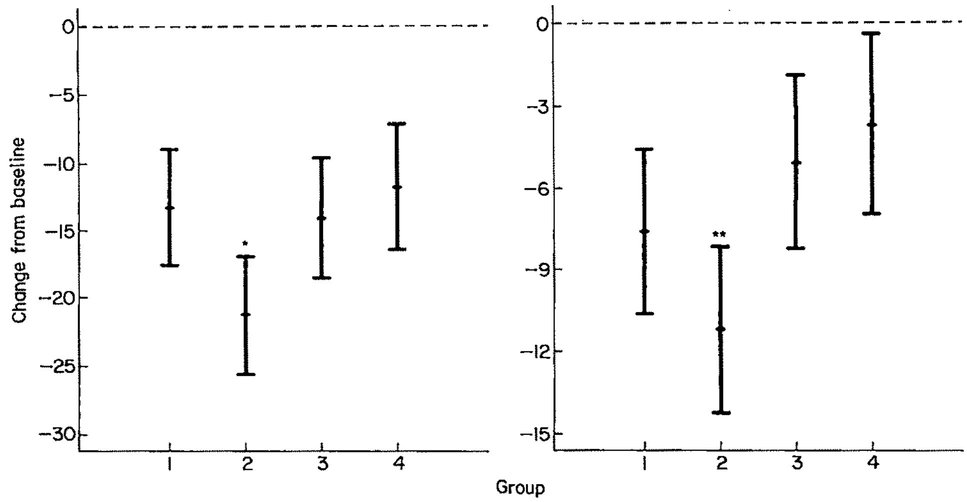

Fig. 4. Psychometric changes at 30 minutes postoperatively showing mean change from baseline and 95% confidence intervals for all groups. * $p < 0.05$; ** $p < 0.01$ (ANOVA). *Left-hand graph:* digital symbol modalities test; *right-hand graph:* p-deletion lines completed.

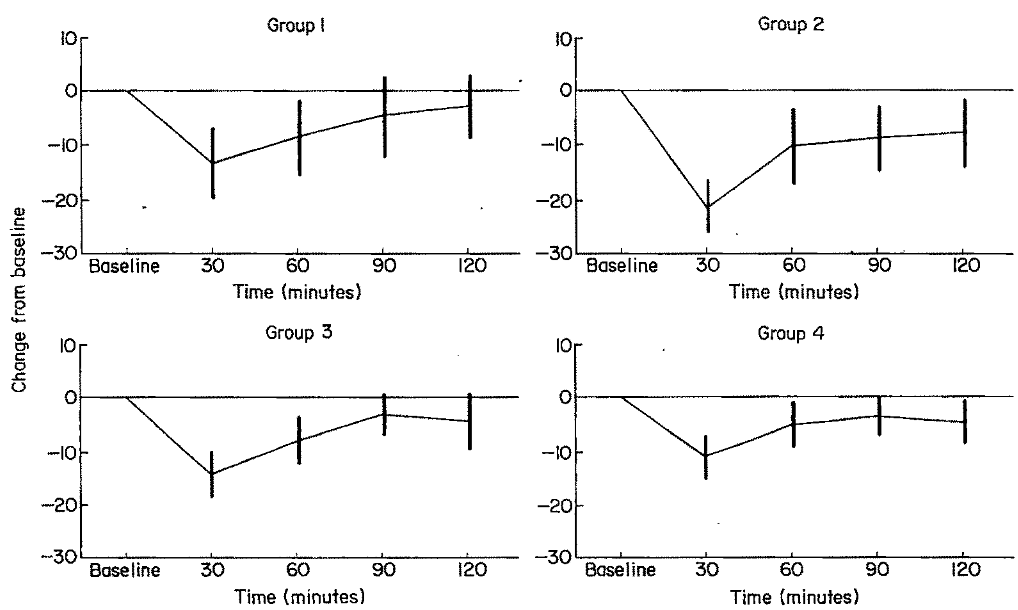

Fig. 5. Psychometric test results showing mean change from baseline and 95% confidence intervals in all groups at each time interval for the digit symbol modalities test.

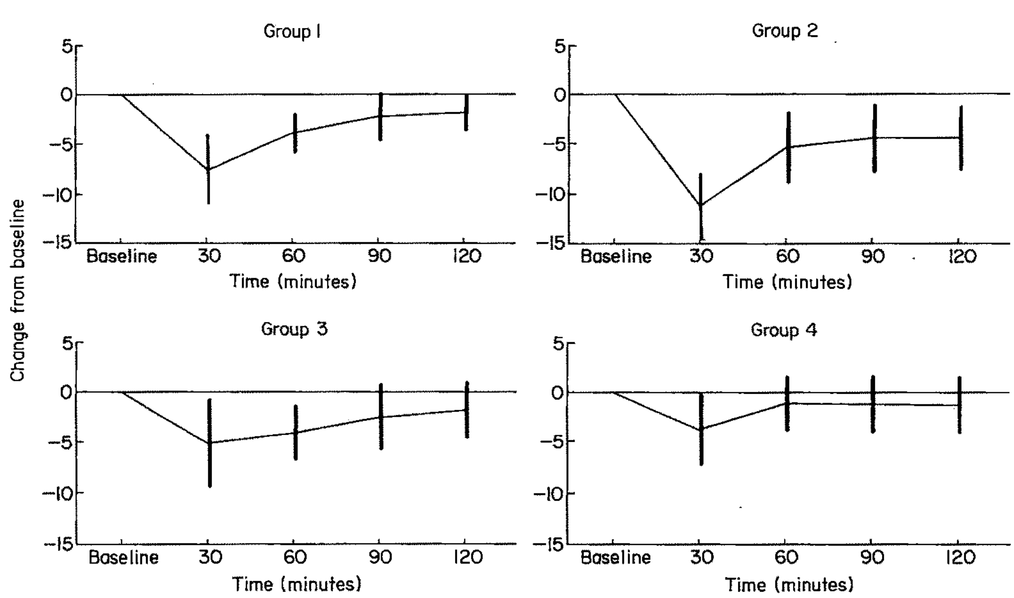

Fig. 6. Psychometric test results showing mean change from baseline and 95% confidence intervals in all groups at each time interval for the 'p' deletion with lines completed.

Table 8. Postoperative visual analogue pain scores. Values expressed in mm as mean (range).

Time interval; minutes	Group 1	Group 2	Group 3	Group 4
30	31 (3–76)	40 (0–89)	32 (0–96)	28 (0–61)
60	32 (4–72)	35 (0–79)	23 (0–73)	26 (1–77)
90	22 (0–83)	24 (0–89)	25 (0–90)	19 (0–62)
120	24 (0–90)	32 (0–86)	25 (0–75)	23 (0–56)

day. Of the others, there was no intra-operative recall in any patient and the only complaints were of a sore throat in 14 patients (group 1:4, group 2:1, group 3:5, group 4:4), headache in 10 patients (groups 1 and 3:4, groups 2 and 4:1) and muscular pains in three patients (group 3:2, group 4:1).

Laboratory investigations

One patient in group 2 had an alkaline phosphatase greater than 1000 U/litre measured in both pre- and postoperative samples; he was referred for further investigation. In the other patients the biochemical, haematological and urine analysis, both before and after operation were all within normal limits except for two diabetic patients who had glycosuria and marginally raised blood glucose levels. There was no difference between the groups in the change from pre- to postoperative values, with the exception of the neutrophil count. In group 2 there was a small decrease in the average neutrophil count whilst in groups 1, 3 and 4 the average count increased ($p < 0.05$ ANOVA). Overall, there was a significant change with a decrease in postoperative values as compared with pre-operative values for the red cell count, haemoglobin, haematocrit, lymphocytes, sodium, total bilirubin, aspartate transaminase, alanine transaminase, alkaline phosphatase, albumin, calcium and urinary specific gravity. There was a concomitant increase in values for the total white cell count, neutrophils, potassium, chlorine and urinary pH. There was no change in the monocytes, basophils, platelets, prothrombin time, urea, creatinine and bicarbonate values (paired *t*-test).

Discussion

It has been stated that 'the ability to deliver a safe, effective general anaesthetic with minimal side effects and achieve a rapid recovery is critically important in the outpatient setting'.[7] The characteristics of desflurane with a blood/gas partition coefficient of 0.42,[1] rapid uptake and elimination,[8,9] lack of toxicity[3,10] and, cardiovascular stability[2] suggest that it would be a suitable agent for induction and maintenance of anaesthesia, providing a rapid recovery and so fulfilling the above criteria.

Induction of anaesthesia with desflurane was accomplished in approximately 2 minutes, as judged by loss of the eyelash reflex and loss of response to verbal commands; however, it caused coughing and excitation in some patients. The excitation phase was of short duration, despite the administration of no premedication and the addition of nitrous oxide helped to alleviate this presumably because the second gas effect enhanced the uptake of desflurane and because of the anaesthetic effect of nitrous oxide itself. There were only three patients (10%) in whom gaseous induction was not tolerated; one of these could not tolerate the facemask even at the pre-oxygenation stage, and the other two had a markedly exaggerated excitation phase with coughing. In the remainder of the patients desflurane induced anaesthesia rapidly; awareness was lost after 3–4 breaths, which was before loss of consciousness was apparent to the anaesthetist. There was a rise in both the systolic and diastolic blood pressure during induction with desflurane which quickly settled. Desflurane provided haemodynamic stability after the initial surgical stimulus. Assisted ventilation was easy and the end-tidal concentration of desflurane could rapidly be changed to adjust the depth of anaesthesia. The use of non-depolarising muscle relaxants in the patients given desflurane was significantly less than in patients receiving propofol for maintenance. The differing requirement of neuromuscular relaxation is likely to be the result of both respiratory depression and an effect at the neuromuscular junction, in common with the other halogenated ethers isoflurane and enflurane.[11]

The propofol infusion regimen used in this study is similar to others used before with unpremedicated patients.[12,13] Seven patients had an episode of bradycardia, which responded to atropine, and nine had an episode of self limiting nodal rhythm causing no cardiovascular embarrassment. The bradycardias tended to occur towards the end of the induction sequence after the administration of fentanyl and before any surgical stimulation. Fentanyl and suxamethonium[14,15] are known to cause bradycardia and may have been contributory factors.

The recovery in patients receiving desflurane for both induction and maintenance was always faster than the patients receiving propofol, either for induction or with an infusion for maintenance. Whilst there is no ideal test of recovery the psychomotor tests which we used have been described.[16-19] The p-deletion test assesses the patient's vigilance in performing a repetitive task. The digit-symbol modalities test is derived from the digit-symbol substitution test of Wechsler's Adult Intelligence Scale.[18,19] It involves a greater degree of memory and tests the ability to perceive relationships and to use symbols. The patients who received propofol for induction and maintenance made a significantly slower recovery than the other groups and even after 2 hours had not returned to their baseline pre-operative values, although all patients were sufficiently awake at 30 minutes to complete the tests.

The overall quality of recovery was similar in all groups. There was a tendency to a higher incidence of nausea and vomiting in patients who received desflurane, but this was worse in those who also had nitrous oxide. This latter is thought to have an emetic effect[20] in addition to which propofol has an antiemetic effect.[21,22] Only one patient in group 2 had an episode of nausea, compared with four patients in group 3. Only patients who received both desflurane and nitrous oxide experienced vomiting.

The other complaints were minor sequelae, commonly seen after general anaesthesia and likely to be from the tracheal tube and the use of suxamethonium.The admission to the ward of seven patients for surgical reasons emphasises the need for adequate back-up facilities for day case patients.

In summary, desflurane has been shown to provide rapid induction and fast recovery from anaesthesia with no serious side effects. The recovery parameters with desflurane tended to be faster than with propofol. These suggest that desflurane would be a suitable agent for day case anaesthesia providing a safe general anaesthetic and a more rapid recovery from anaesthesia.

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Lumbar regional anaesthesia and prophylactic anticoagulant therapy

Is the combination safe?

P. WILLE-JØRGENSEN, L. N. JØRGENSEN AND L. S. RASMUSSEN

Summary

A survey has been carried out in all Danish anaesthetic departments (n = 80) regarding the attitude towards the use of epidural/spinal lumbar analgesia in patients who were receiving prophylactic anticoagulant therapy for the prevention of thromboembolism. About 60% of the departments used the techniques in patients receiving low-dose heparin and no side effects had been experienced. Spinal and epidural anaesthesia were in general regarded as being contraindicated in patients fully anticoagulated with vitamin K antagonists. In the world literature, the attitude towards the combination is conflicting. No randomised trial has been performed and complications are almost entirely confined to patients fully anticoagulated with vitamin K antagonists. Only one case of an epidural haematoma has been recorded when subcutaneous low-dose heparin was used as thromboprophylaxis.

Key words

Anaesthetic techniques, regional; spinal, epidural.
Blood, anticoagulants; heparin, warfarin.
Complications; haematoma, thromboembolism.

Haemorrhage into the epidural or subarachnoid space always implies a risk of serious disablement. It is either spontaneous or secondary to coagulation defects including anticoagulation treatment, vascular malformations or neoplasia. Occasionally, iatrogenic haemorrhage is seen after anaesthetic or diagnostic puncture.[1–4] The reported incidence of blood vessel puncture following insertion of epidural catheters is between 1 and 11%,[1,5–7] but this complication is seldom accompanied by any symptoms. Since 1952 at least 100 cases of epidural haematoma following epidural anaesthesia have been described in patients receiving full anticoagulation.[8,9] Following spinal anaesthesia or diagnostic lumbar puncture at least 33 cases of subarachnoid haemorrhage have been reported.[4]

Low-dose heparin is widely used prophylactically in Danish surgical patients,[10] and has been shown to reduce the incidence of fatal pulmonary embolism.[11] The use of these regional techniques reduces morbidity after surgery of the lower abdomen and legs.[12] There is a general consensus that regional anaesthesia is contraindicated in patients receiving full anticoagulation therapy,[1,13–15] but its safety in combination with low-dose heparin or dextran remains controversial.[1–4]

In orthopedic surgery epidural or spinal anaesthesia reduce the incidence of postoperative deep venous thrombosis,[16] as does the use of heparin.[11] No randomised investigations have focused on the possible synergistic thromboprophylactic effect of these regional techniques combined with antithrombotic drugs. In general surgery, no thromboprophylactic effect has been found with the use of thoracal epidural blockade,[17] but a favourable effect on morbidity has been documented.[12] As the use of medical thromboprophylaxis in these patients is also necessary, the combined treatment may be justified. In vascular surgery the use of heparin is essential and, again, as the use of regional anaesthesia lowers morbidity, the combination may be useful.

In most kinds of surgery, the use of epidural or spinal anaesthesia in patients receiving prophylactic anticoagulants remains a therapeutic dilemma;[1,18] i.e. a theoretical risk of serious bleeding versus the benefit from the use of regional blockade and thromboprophylaxis.

We have evaluated the attitude of Danish anaesthetists to this dilemma by means of a questionnaire. We have also attempted to clarify the relative roles of vitamin K antagonists, heparin, dextran and aspirin in the possible develop-

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Table 1. Questionnaire used.

1.	How many epidural and spinal anaesthetics were given in 1988?
2.	What kind of medical thrombosis prophylaxis is routinely used in orthopaedic, general surgical, and gynaecological patients: Low dose heparin, dextran, others, or none?
3(a)	If an epidural catheter is inserted before surgery, the use of heparin 5000 IU subcutaneously twice daily is: contraindicated (1 point), relatively contraindicated (2 points), not contraindicated (3 points).
(b and c)	Same question for administration of dextran (4×500 ml) or aspirin (250 mg daily).
4.	As 3, but for the use of spinal analgesia.
5(a)	Is there a lower limit for prothrombin/proconvertin (PP) levels below which epidural analgesia is contraindicated?
(b)	Same question for the use of spinal analgesia. Yes, value? or No.
6(a)	Has anyone in your department ever experienced verified cases of epidural or subarachnoid bleeding causing symptoms which could be related to the use of thrombosis prophylaxis after introduction of an epidural catheter?
(b)	Same question for spinal analgesia.
7.	Comments

ment of haematoma formation. The literature has also been reviewed in order to evaluate this risk of epidural or subarachnoid haemorrhage following their use.

Methods

A questionnaire (Table 1) was sent to all departments of anaesthesia in Denmark ($n = 80$). The attitude towards the use of epidural or spinal anaesthesia in different clinical situations (question 3) was evaluated by using the following scoring system: absolutely contraindicated: 1; relatively contraindicated: 2; not contraindicated: 3. Wilcoxon's test for paired data in 2 groups and Spearman's test for rank correlation were used for statistical analysis. The sign test was used for comparison of the preference of the departments for thrombosis prophylaxis in different categories of patients. A two-sided level of significance at 5% is used, and materials are shown with median and 95-interpercentile range.

Table 2. Number of departments in which epidural or spinal anaesthesia are regarded as being absolutely or relatively contraindicated in patients receiving low dose heparin therapy. (Any discrepancies in numbers are due to departments not using heparin or that particular question not being answered).

	Number of departments	Total points score
Absolutely contraindicated		
epidural	7 (11%)	7
spinal	4 (6%)	4
Relatively contraindicated		
epidural	18 (27%)	36
spinal	12 (18%)	24
Not contraindicated		
epidural	39 (59%)	117
spinal	50 (76%)	150

Results

Seventy four (93%) departments returned the questionnaire, but eight were inadequately completed, thus leaving a response rate of 83%. In 1988 these departments used epidural analgesia on an average of 95 occasions (range 0–200) and spinal anaesthesia on an average of 250 times (2–2000).

Twenty departments (30%) reported that thrombosis prohylaxis was used for selected patients only. The most frequently used was low-dose subcutaneous heparin (5000 units twice daily) (Fig. 1). The number of departments which regarded epidural or spinal anaesthesia as being absolutely or relatively contraindicated in patients receiving prophylactic heparin therapy is shown in Table 2. Twenty-five departments (38%) regarded low-dose heparin therapy as being a relative or absolute contraindication to epidural anaesthesia, but only 16 departments (24%) regarded spinal anaesthesia as being relatively or absolutely contraindicated under these circumstances (Fig. 2). A liberal attitude towards the use of epidural anaesthesia,

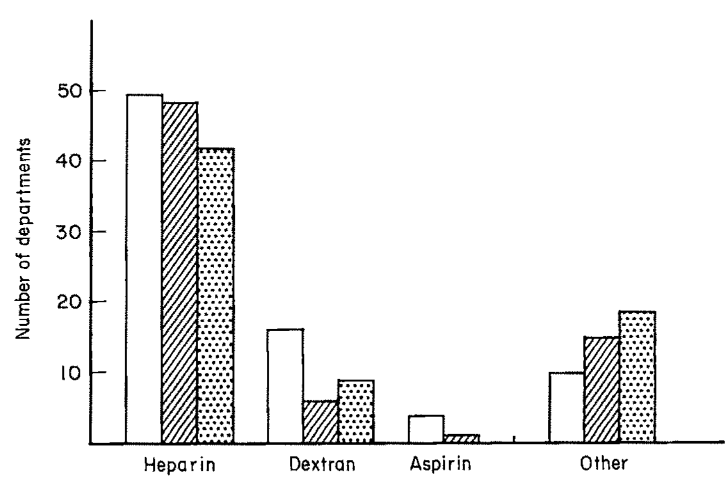

Fig. 1. Routinely used thrombosis prophylaxis for orthopedic surgery, □; general surgery, ▨; gynecology, ▩.

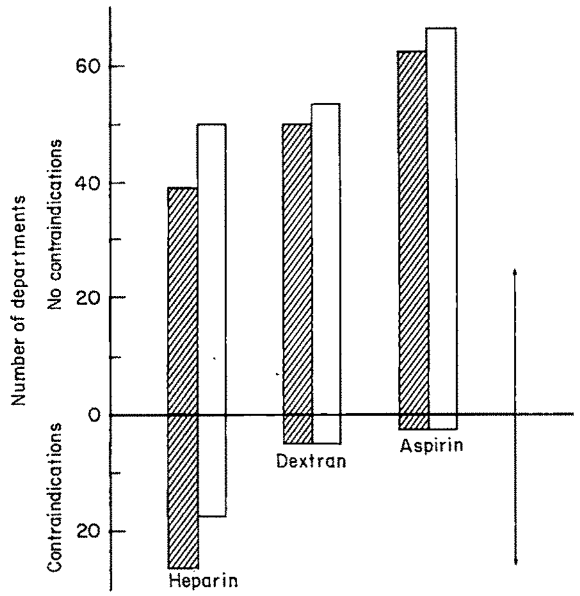

Fig. 2. The attitude of Danish anaesthesiological departments towards the use of epidural analgesia (EA), ▨; and spinal analgesia (SA), □ if medical thromboprophylaxis is used.

expressed as the number of points from question 3 showed a weak positive correlation to the total number of epidurals and spinals performed in each department. ($r(s) = 0.29$, $p = 0.03$).

Epidural or spinal anaesthesia was not regarded as being absolutely contraindicated by any department when dextran or aspirin was used, but was a relative contraindication in 3% and 6% respectively.

Eight and 11 departments respectively did not mention any level of prothrombin/proconvertin (PP) below which the use of epidural and spinal was contraindicated. For the other departments the median PP level was 40% (range 15–86) for epidural and 31% (range 15–100) for spinal anaesthesia. Eight percent of departments performed epidural anaesthesia with a PP below 20%, as did 12% with regard to spinal anaesthesia. The acceptable level was significantly lower for the spinal route ($p < 0.001$).

Two departments answered yes to question 6.

Patient 1. A 68-year-old male with a complicated tibial fracture was anticoagulated with phenprocoumone. Twenty days later external fixation was planned, and, as the anaesthetist was unaware of the anticoagulant therapy, epidural anaesthesia was used. A catheter was inserted, with difficulty, 5 cm cranially at the L_{3-4} interspace; no bleeding was observed during the procedure. A satisfactory block was obtained and surgery completed. Three days later the patient developed paresis of the bladder and the rectal sphincter and paresis, areflexia, and hyposensibility of the lower extremities. The PP was found to be 10% and the anticoagulation was stopped. An epidural haematoma was evacuated from the T_{11}–L_1 level. The paresis of the extremities was irreversible.

Patient 2. An 83-year-old woman had a pin and plate for a left femoral neck fracture under a single shot spinal anaesthetic at what was thought to be the L_2–L_3 interspace. The block was technically difficult because of obesity and severe osteoarthritis of the lumbar spine. No bleeding was observed. The operation and immediate recovery were smooth, but 36 hours after surgery she complained of severe pain in the right lumbar region radiating to the knee; there were no abnormal neurological signs. Deep venous thrombosis was suspected and treatment with heparin 15 000 units intravenously followed by 10 000 units 4 times daily was commenced. Eleven hours later she complained of pain in both arms and the back. Analgesia, areflexia and paresis of both legs were found. The PP was 18% and the activated partial thromboplastin time 122 seconds. After injection of protamine 50 mg, lumbar myeolography revealed a total stop of contrast medium at the L_1 level. Due to her poor condition, no further treatment was advised and she died 6 days after the primary operation. At postmortem examination the subarachnoid space was completely filled with blood and the perforation of the dura was found just above L_1.

Discussion

In both orthopaedic and general surgery the benefits of thromboprophylaxis[11] and the use of regional anaesthesia[12] are well known, but the simultaneous use of both regimens is controversial. The results of our questionnaire show that both prophylactic anticoagulant therapy and regional anaesthesia are widely practiced in Denmark, but the attitude towards using both methods simultaneously varies widely. Those departments which use epidural and spinal anaesthesia frequently are much more liberal in their approach to using lumbar regional anaesthesia in patients receiving prophylactic anticoagulants. Some units practice epidural anaesthesia with PP values as low as 15%, while others demand normal values. In only two documented instances did bleeding into the epidural or subarachinoid space produce symptoms, but both these patients were fully anticoagulated, one with a vitamin K antagonist and the other high-dose heparin.

There is no information on the incidence of symptomatic and nonsymptomatic haematomas after regional anaesthesia. The majority of the former have occurred spontaneously[8] and are seen in patients both with and without anticoagulation.[4] More than 100 cases of epidural or subarachnoid haematomas are described after epidural and spinal anaesthesia. About one third of these patients had an abnormal coagulation status.[4,9] Six cases of haematomas after spinal anaesthesia are reported, but only one of these occurred without multiple attempts at dural puncture or known coagulation disorders.[4] The incidence of haematomas after epidural anaesthesia appears to be very low, but the exact figure is not known due to problems with diagnosis.[8,18,19] In a larger series the incidence of irreversible neurological damage after epidural anaesthesia, but not confined to haematomas, was about 1 per 10 000.[20]

No prospective randomised trial has been done to evaluate the risk of performing spinal or epidural blocks in patients receiving prophylactic anticoagulants. However, several cases of epidural haematoma[8,3,14,21,22] or subarachnoid bleeding[1,4] have been recorded following epidural or spinal anaesthesia in patients receiving vitamin-K antagonists, but in almost all the reports the degree of anticoagulation is described inadequately. The conclusions were that treatment with vitamin K antagonists in therapeutic doses is a contraindication to the use of lumbar regional anaesthesia. In a series of 950 patients undergoing

vascular surgery,[9] an epidural catheter was inserted before surgery. The patients had received oral anticoagulants if they were not treated with aspirin or if they suffered from thrombocytopenia. The mean plasma levels of Factor II, VII and X were 19% (range 10–52) (Thrombotest, normal therapeutic range 5–10%). During surgery 200–400 IU of heparin were used intra-arterially and additional heparin was infused until the partial thromboplastin time was four times the pre-operative value. Despite this intensive therapy no patients developed an epidural haematoma that caused neurological symptoms.

Thus it would appear that the risk of a haematoma after epidural or spinal anaesthesia in an anticoagulated patient has not been shown to be greater than the risk of one occurring spontaneously. Nevertheless, the general opinion would be not to recommend regional anaesthesia in patients receiving full anticoagulant doses of vitamin K antagonists.[1,13,14]

An epidural haematoma has been discribed in one patient who was receiving 5000 IU heparin intravenously three times a day. The first dose was administered following insertion of the epidural catheter.[13] During the next 3 days progressive paralysis and sensory loss occurred in the lower extremities and a haematoma was evacuated at laminectomy from the L_{2-4} level. All reported cases of bleeding into the lumbar epidural or subarachnoid space with neurological defects have occurred when heparin was administered intravenously in bolus doses.[4,13,14,21–23] The episodes have been reported both when heparin was administered before and after the lumbar block. To our knowledge, only one case has been recorded of a symptomatic haematoma following subcutaneous low-dose prophylactic heparin therapy (5000 units twice daily) in a patient who had epidural anaesthesia.[24] This occurred 4 hours after heparin administration when an epidural catheter was inserted for postoperative pain relief. Several attempts at catheter placement were made, and when introducing the catheter reflux of blood was observed. The patient complained of sudden pain in the legs, which was followed by complete paraplegia. Evacuation of a haematoma from T_{10}–L_5 did not correct the neurological defects. The pre-operative coagulation status was normal. The fact that repeated punctures were necessary and the bleeding occurred shortly after the puncture suggests that the reason for the bleeding was mechanical rather than medical.

Despite the extreme rarity of these complications, some authors warn against the use of epidural anaesthesia in patients treated with low-dose heparin, since there is no reliable method for monitoring the risk of bleeding.[4,25] In vascular surgery continuous epidural anaesthesia was used in 912 patients who had an intra-operative bolus injection of 75 IU heparin/kg followed by 1000 IU/hour intravenously.[26] No side effects were observed and it was concluded that the advantages obtained from the epidural outweighed the risk of haematoma formation. In another study, no complications were reported in 100 patients who underwent vascular surgery with epidural anaesthesia and who were heparinised intra-operatively.[27] No untoward effects were seen. Low-dose heparin (5000 IU twice daily subcutaneously) was started before use of epidural or spinal anaesthesia in 187 orthopedic[28] and 136 general surgical patients.[15] The regimen was continued after surgery. In the latter group the epidural catheter remained *in situ* for 3 days postoperatively and was removed regardless of the interval since the last injection of heparin. No side effects were recorded. In 4011 vascular surgical patients epidural or spinal block were performed if no coagulation disorders were present. If no fresh bleeding occurred during cannulation, the block proceeded and heparin was given intravenously during surgery until the partial thromboplastin time was doubled. After surgery, 2600 IU of heparin was administered intravenously every 6 hours. The catheter was removed 24 hours later just before the next dose of heparin administration. No side effects were reported.[29] It is difficult to draw conclusions from the occasional reports describing bleeding complications after heparinisation.[13,14,22,23] It is probable that not all cases have been reported. The newer series reported in patients undergoing vascular surgery show that the combined regimen appears to be safe, even when heparin is administered intravenously, if properly monitored. Low-dose heparin is widely used in Denmark and the results of this survey show that more than 60% of Danish anaesthetists use regional anaesthesia together with low-dose heparin. Apparently, this combination regimen has not resulted in any spinal or epidural haematomas. To our knowledge only one case of an epidural haematoma has been recorded in a patient receiving subcutaneous low-dose heparin. Thus, it would be reasonable to assume that the combination of subcutaneous low-dose heparin and epidural or spinal anaesthesia is safe if the patient does not suffer from a bleeding disorder. A randomised clinical investigation to give the final answer is not feasible, as the number of probands would have to exceed more than 100 000.

Aspirin and other prostaglandin antagonists interfere with platelet function and increase postoperative blood loss.[2] It is unknown whether the use of these drugs elevates the risk of subarachnoid bleeding.[4] A few cases of spontaneous or traumatic epidural haematomas have been reported.[30,31] In a retrospective study, peri-operative antiplatelet therapy was associated with aspiration of blood through the spinal or epidural needle. However, the authors concluded that patients receiving antiplatelet therapy can safely undergo major regional anaesthesia, provided that they are closely monitored in the peri-operative period for early signs of cord compression.[32] As these drugs are so widely used, the risk of this complication can be ignored for all practical purposes. There is no information whether the use of dextran enhances the risk of epidural or subarachnoid bleeding.

We conclude that most symptom-giving haematomas after epidural and spinal anaesthesia are found in the epidural space. In patients fully anticoagulated with vitamin K antagonists regional anaesthesia of this type is not recommended. Their combination with intravenous heparin is controversial, but has been found safe if the activity of heparin is closely monitored with the partial thromboplastin time. The use of subcutaneous low-dose heparin, aspirin, or dextran for prophylactic anticoagulant therapy are not in themselves a contraindication against the use of epidural or spinal anaesthesia.

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Comparison of the combined effects of atropine and neostigmine with atropine and edrophonium on the lower oesophageal sphincter

S. A. M. HEIJKE, G. SMITH AND A. KEY

Summary

In two groups (n = 11) of healthy patients, we have measured gastric, lower oesophageal and barrier pressures before and after antagonism of neuromuscular block during anaesthesia with nitrous oxide and isoflurane. In one group, atropine 1.2 mg and neostigmine 2.5 mg were given and in the second group atropine 0.6 mg with edrophonium 1 mg/kg. One minute after administration of the reversal agents, there was a significantly greater reduction in barrier pressures in the neostigmine and atropine group than in the edrophonium and atropine group, but subsequently, there was no significant difference between the two groups. We conclude that there is no clinical difference between the two reversal mixtures in terms of the risk of regurgitation in the immediate period after reversal.

Key words

Antagonists, neuromuscular relaxants; edrophonium, neostigmine.
Gastrointestinal tract; oesophagus.
Complications; regurgitation.

It is generally accepted that the lower oesophageal sphincter (LOS) is the main barrier in preventing gastro-oesophageal regurgitation[1] and the tendency to regurgitation is opposed by the barrier pressure (BrP), which is the difference between LOS pressure (LOSP) and gastric pressure (GP). Thus it is known that patients with hiatus hernia with the most marked degree of gastro-oesophageal reflux have the lowest barrier pressures and there is a relationship between the degree of reflux and sphincter pressure.[2]

Since gastro-oesphageal reflux and aspiration of gastric contents is known to occur not only during induction of anaesthesia, but also during recovery from anaesthesia, several studies have examined the changes in barrier pressure which occur on termination of anaesthesia. These have been done, in particular, when residual neuromuscular block is antagonised with combinations of cholinergic drugs[3] which increase BrP and anticholinergics which decrease BrP. In one study, it was demonstrated that a mixture of atropine 1.2 mg and neostigmine 2.5 mg did not alter barrier pressure significantly, but when the dose of neostigmine was increased to 5 mg, there was a significant increase in barrier pressure.[4] Similar results were found when glycopyrronium was used instead of atropine.[5]

Edrophonium may be used as a substitute for neostigmine to antagonise residual nondepolarising neuromuscular block. It has a similar duration of action to equipotent doses of neostigmine, but the advantage of a more rapid onset of action and reduced requirements for atropine. As far as we know, there have been no previous investigations of the effect of edrophonium on the LOS during anaesthesia.

The purpose of the present study was to compare the effects of two commonly used reversal mixtures (atropine 1.2 mg with neostigmine 2.5 mg and atropine 0.6 mg with edrophonium 1 mg/kg) on the lower oesophageal sphincter.

Method

Following approval by the District Ethics Committee and after obtaining informed patient consent, we studied 22 healthy female patients undergoing elective gynaecological surgery. No patient was obese and none had symptoms of gastro-oesophageal reflux or was taking any medication known to interfere with the gastrointestinal tract. Where appropriate, patients were requested to refrain from smoking for at least 8 hours, the duration of pre-operative fasting.

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Premedication was with diazepam 10 mg orally 2 hours before anaesthesia[6] which was induced with thiopentone 4 mg/kg. Atracurium 0.4 mg/kg was administered to facilitate tracheal intubation[7] and the patient's lungs were ventilated with nitrous oxide 70% and isoflurane 0.5–1% in oxygen. Ventilation was adjusted to maintain normocapnia as measured by end-tidal carbon dioxide monitoring (Datex Normocap). Morphine sulphate 10 mg was given to all patients shortly after induction, as an adjuvant to anaesthesia.[8]

Towards the end of surgery, an oesophageal manometry tube was passed through the oesophagus into the stomach. This tube consists of a 3-mm orogastric tube into which is embedded three sensitive subminiature strain gauge pressure transducers at 5, 10 and 15 cm from the tip (Gaeltec Ltd, Isle of Skye, Scotland). In all instances, the system has been shown to remain stable. The transducers were attached via pre-amplifiers to a chart recorder to produce a permanent record of the pressures. Before each investigation, the manometer system was calibrated in a column of water and at the end of the investigation, calibration was repeated to exclude significant zero baseline or calibration drift.

After insertion of the three transducers into the stomach, baseline measurements of GP, LOSP, and oesophageal pressures were measured sequentially at the end of expiration, as the transducers were withdrawn slowly from the stomach into the oesophagus. This pull-through manoeuvre[8] was performed three times before administration of the reversal mixture and repeated at 1-minute intervals for 16 minutes after reversal, while anaesthesia was maintained with nitrous oxide and isoflurane in oxygen to avoid coughing or straining.

Patients were allocated at random to receive a combination of atropine 1.2 mg and neostigmine 2.5 mg (group N/A) or atropine 0.6 mg and edrophonium 1 mg/kg (group E/A) as a bolus when at least one twitch could be elicited on peripheral nerve stimulation.[9,10]

The percentage change in BrP from baseline was calculated and data were analysed statistically using MANOVA. Differences between groups were analysed by Student's *t*-test and a p value of less than 0.05 was taken as significant.

Results

There were no significant differences between the two groups in age, weight or baseline values of GP, LOSP or BrP (Table 1).

Following administration of the reversal mixture, in the E/A group, there was a significant increase in BrP at one minute of 8.7% (10.2) (mean (SD)). However, in the N/A group, BrP decreased immediately and consequently there was a significant difference between the two groups at one minute.

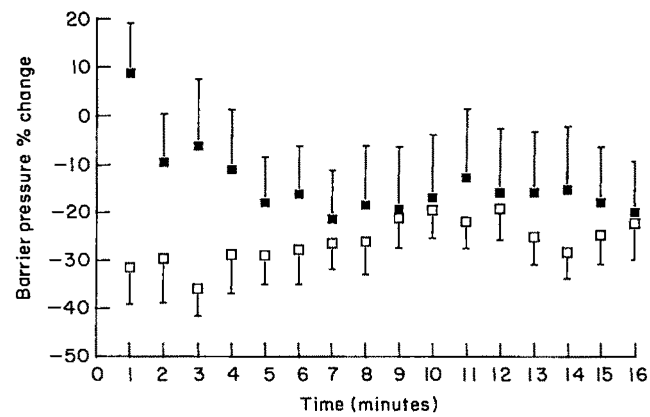

Fig. 1. Percentage change in BrP produced by the simultaneous administration of atropine 1.2 mg and neostigmine 2.5 mg (lower profile, □) or atropine 0.6 mg and edrophonium 1 mg/kg (upper profile, ■). For clarity the mean and SEM in only one direction has been shown.

After one minute BrP was decreased significantly in both groups, compared with control values, but there was no significant difference between the two groups (Fig. 1). Throughout this period, there was only minimal increase in gastric pressure (approximately 2 cm H_2O) and the major reduction in BrP was caused therefore by a reduction in LOSP in both groups.

There were no differences between the two groups in the lowest value of BrP measured, percentage decrease from baseline or the time at which the lowest value was recorded. Although the time to the lowest value was of the order of 5–6 minutes, there was considerable variation between patients (Table 2).

Some patients who received the edrophonium/atropine mixture had a reduction in heart rate shortly after administration, but this was transient, of no clinical significance, and did not require treatment.

Discussion

Regurgitation and pulmonary aspiration during or after anaesthesia are passive processes and are dependent upon relaxation of both upper and lower oesophageal sphincters. It is generally accepted with gastro-oesophageal regurgitation that the tone in the LOS is the main protective barrier preventing regurgitation. There is great variation in both LOSP and BrP between normal individuals and it is not possible therefore to define a threshold level of BrP below which regurgitation occurs. Nevertheless, it is known that reflux occurs to a greater degree in patients with the

Table 1. Patient characteristics and control values of GP, LOSP and BP (mean (SD), apart from age).

	E/A group	N/A group
Age; years	30.8 (range 24–36)	33 (range 26–48)
Weight; kg	56.9 (7.0)	62 (11.1)
Gastric pressure	8.4 (3.6)	8.8 (3.1)
LOSP	46.0 (17.7)	51.3 (18.4)
BrP	37.4 (16.1)	42.5 (17.0)

Table 2. Comparison of time to lowest value of BrP, actual lowest value of BrP, and lowest value as a percentage of control value between atropine 1.2 mg and neostigmine 2.5 mg (N/A) or atropine 0.6 mg and edrophonium 1 mg/kg (E/A) (mean+SD).

	BrP lowest value (cm H_2O)	Lowest value (% control)	Time to lowest value (minutes)
E/A	25.2 (16.5)	−34.7 (30.3)	6.7 (4.2)
N/A	22.3 (12.5)	−42.5 (19.0)	5.8 (4.5)

lowest sphincter pressures and it seems logical therefore that a reduction in BrP will enhance any tendency to regurgitation.

Previous studies have shown that a mixture of atropine 1.2 mg with neostigmine 2.5 mg caused a transient reduction in LOSP but that 3 minutes later, there was no significant difference compared with baseline. In a study on pregnant women undergoing elective Caesarean section, Brocke-Utne and colleagues found that atropine 1.2 mg and neostigmine 2.5 mg resulted in a slight non-significant decrease in LOSP[11] but doubling the dose of neostigmine caused a significant increase in LOSP and BrP, one minute after administration of the mixture.

It has been suggested that edrophonium is preferable to neostigmine for antagonising neuromuscular blocking drugs as it has a more rapid onset of action and weaker muscarinic effects. Since atropine has been shown to reduce significantly both LOSP and BrP, it would be advantageous to keep the dose of this drug as low as possible; it has been stated that if edrophonium is used, the usual dose of atropine may be halved.[12]

The recommended method of administration of edrophonium is in divided doses, 0.2 mg/kg followed one minute later by 0.8 mg/kg for antagonism of more than 90% depression of train-of-four induced by atracurium, although this negates one of the advantages of the use of edrophonium, namely a more rapid onset of action.[13] Edrophonium is known to be less effective than neostigmine in antagonising profound block induced by pancuronium[14,15] and even supraclinical concentrations of the drug do not completely antagonise more than 95% depression of train-of-four.

Very high concentrations of anticholinesterases produce random hyperactivity, manifested by spontaneous twitching and repetitive firing with severe fade on stimulation, so doses of edrophonium >1 mg/kg should probably be avoided.[16]

Potency of reversal agents differs for different muscle relaxants[17] and potency ratios probably depend also on the end point chosen for full neuromuscular recovery.[18] At 95% block the edrophonium/neostigmine potency ratio is approximately 35 : 1[19] whereas at lesser degrees of block, the ratio is as little as 12 : 1.[12,20] Certainly as little as 0.5 mg/kg does not consistently antagonise block induced by vecuronium, particularly if there are fewer than four responses to train-of-four.[21]

Although the action of edrophonium is maximum 0.8 to 2 minutes after administration, many investigators have used it in a mixture with atropine without adverse effects on heart rate.[22]

We selected atropine as the anticholinergic agent as adminstration of an atropine/edrophonium mixture was found to produce better stability of heart rate compared with a mixture of glycopyrronium and edrophonium.[23] When given in equipotent doses, neostigmine and edrophonium have a similar duration of action because their rates of elimination are similar.

In this study, we found that one minute after administration of the reversal mixture, BrP was significantly higher following the E/A mixture, but subsequently there was no significant difference in barrier pressure between the two groups. It is noteworthy that in this investigation, barrier pressure remained significantly lower than baseline from 2 minutes onwards to the termination of the study, whereas in our previous investigation, following administration of atropine and neostigmine, there was a transient reduction in barrier pressure, which lasted only 3 minutes and subsequently there was no significant difference in barrier pressure compared with baseline. However, in our former investigation anaesthesia was maintained with enflurane whilst in the present investigation, anaesthesia was maintained with isoflurane.

We conclude that in terms of prevention of regurgitation in the immediate postreversal period, the use of edrophonium has no advantage in comparison with neostigmine in the doses administered.

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The effects of intravenous clonidine on ventilation

R. OOI, J. PATTISON AND S. A. FELDMAN

Summary

The effects of clonidine, an alpha 2 adrenergic agonist, on ventilation were studied in a group of adult volunteers. The ventilatory variables measured were minute ventilation, respiratory rate, end-tidal carbon dioxide tension and the response to carbon dioxide challenge. We found no differences in minute ventilation, respiratory rate and end-tidal carbon dioxide tension, before and after clonidine administration. However, the ventilatory response to carbon dioxide was significantly attenuated following clonidine, suggesting that clonidine has respiratory depressant effects.

Key words

Ventilation; Pharmacology; clonidine.

There is growing interest in the use of clonidine, an alpha-2 adrenergic agonist, as an adjunct to anaesthetic agents. Clonidine has been shown to produce a reduction in anaesthetic requirements in animals.[1] In humans, it reduces the quantities of anaesthetic and analgesic agents required to obtund the pressor response to laryngoscopy and intubation.[2] It is effective in maintaining haemodynamic stability peri-operatively[3] and has analgesic effects whether given extradurally or parenterally.[4] Clonidine has also been shown to potentiate motor and sensory block when given with bupivacaine intrathecally.[5]

This study was undertaken because of the current interest in clonidine, to evaluate its effects on ventilation in adult volunteers.

Methods

Ten healthy adult volunteers (six males and four females, age range 22–33 years, weight 50–85 kg) participated in the trial, which had ethics committee approval. The study was divided into two stages, with each volunteer acting as his/her own control. The stages were before and 30 minutes after intravenous administration of clonidine 3 μg/kg. The dose range was therefore between 150 and 250 μg.

The volunteers abstained from alcohol and caffeine for 6 hours before the study. Both stages were carried out on the same day with the subjects resting in the recumbent position throughout the experiment. The volunteers breathed through a tight fitting facemask fitted with a non-rebreathing valve (Ambu E). End-tidal carbon dioxide tension ($P\text{E}'\text{CO}_2$) analysis was performed 'on line' by a Hewlett Packard capnometer (model 47210A), via a sensor attached to the expiratory end of the Ambu valve. The capnometer also measured respiratory rate (f). The calibration of the machine was checked at the beginning of the experiment using the manufacturer's standard. The accuracy was referred to a BOC certified carbon dioxide gas mixture. The agreement was $\pm 0.1\%$. Expired minute ventilation ($\dot{V}\text{E}$) was determined by a Wrights respirometer connected in the expiratory limb of the valve. The performance of the respirometer was checked against universal Rotameters (Gapmeter Lab Kit A6 and A10) which had been previously calibrated against a spirometer of known accuracy (Ohio Airco 840). The ventilatory volumes were measured at ambient temperature, pressure and saturation (ATPS).

Each volunteer was allowed up to an hour to become familiar with the breathing system. During carbon dioxide (CO_2) challenge, the subject breathed through the Ambu valve, drawing a fixed concentration of CO_2 in oxygen from a 200 litre capacity reservoir (Douglas) bag. A second prefilled bag was also connected via a two-way valve in case it was required. The subjects inspired three different concentrations of CO_2 (2, 4, 6%) in oxygen during each stage of the experiment. During the CO_2 challenge, $\dot{V}\text{E}$ and $P\text{E}'\text{CO}_2$ readings were taken when $\dot{V}\text{E}$ was reasonably stable. This is usually after 5 minutes of breathing the fixed concentration of CO_2.[6] In our study, the readings were stable between 5 and 12 minutes of inhaling CO_2. The slope of the CO_2 response was obtained by linear regression of the plot of $\dot{V}\text{E}$ against $P\text{E}'\text{CO}_2$.

Statistical analyses were performed using the paired

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Table 1. Resting minute ventilation, end-tidal carbon dioxide values and ventilatory response to CO_2 including the intercepts for the constructed CO_2 response lines. Values are expressed as mean (SEM).

	$\dot{V}E$ (litres/minute)	$PE'CO_2$ (kPa)	$\dot{V}E/PE'CO_2$ (litres/minute/kPa)	INTERCEPT OF $\dot{V}E/PE'CO_2$ (kPa)
Control	7.2 (0.5)	5.3 (0.1)	11.2 (3.5)	5.07 (0.16)
Clonidine	6.8 (0.4)	5.5 (0.1)	*6.1 (1.7)	5.08 (0.33)
95% confidence interval for difference	−1.5 to 0.2	−0.4 to 0.1	0.5 to 9.6	0.4 to 0.7

Control, before clonidine administration; clonidine, 30 minutes following 3 μg/kg; $\dot{V}E$, minute ventilation; $PE'CO_2$, end-tidal carbon dioxide tension; $\dot{V}E/PE'CO_2$, slope of CO_2 response line; *significant at $p < 0.05$.

t-test for $\dot{V}E$, f and $PE'CO_2$. The Wilcoxon paired test was used for the slope of the CO_2 response because the latter is known to be skewed in the normal population.[7] The level of significance chosen was $p < 0.05$.

Results

There were no significant differences in $\dot{V}E$, or $PE'CO_2$ before and after clonidine administration (Table 1). There was however, a significant decrease in the slope of the CO_2 response line after clonidine. The direction of change of this slope is illustrated in Figure 1. From the constructed CO_2 response lines, the calculated intercepts when $\dot{V}E$ was zero, did not show any significant differences comparing the results before and after clonidine.

Blood pressure and heart rate changes were monitored in all the volunteers; before the start of the experiment and at 15 minute intervals following clonidine administration, up to 2 hours. The maximal fall in blood pressure occurred within 30 minutes of giving clonidine; the average drop in systolic pressure was 9% and it was 10% for the diastolic blood pressure. In each case, on no occasion was the decrease greater than 20%; the lowest systolic pressure was 90 mmHg. There was also an accompanying decrease in heart rate of around 10 beats per minute. The biphasic response of an initial rise in blood pressure, which can occur with intravenous clonidine, was not detected.

Besides the haemodynamic changes, all the volunteers experienced the sensation of drowsiness and dry mouth. No other comments or problems were noted.

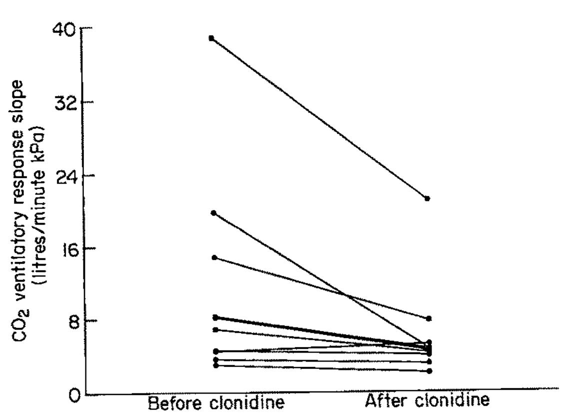

Fig. 1. The effect of clonidine (3 μg/kg) on the slope of the carbon dioxide-ventilatory response.

Discussion

Many anaesthetic drugs, including those used to supplement anaesthesia, have respiratory depressant effects which have been studied extensively both in the laboratory and clinical environment. Despite the current interest in clonidine, there is little available data describing its respiratory effects. Our trial was therefore to assess its effects on respiration.

Our results show that there is no change in f, $\dot{V}E$ or $PE'CO_2$ following clonidine 3 μg. There was, however, a depression of the ventilatory response to CO_2, implying some depression of respiration. The finding of nonsignificant changes in the calculated intercepts for the constructed CO_2 response lines agrees with the nonsignificant changes in resting $\dot{V}E$ and $PE'CO_2$. As the study involved healthy adults, this change can be assumed to be due to an alteration in the central chemoreceptor mechanism. It is possible that clonidine may potentiate the respiratory depression caused by opiates. However, this effect may be offset by the reduced quantities of opioids and other anaesthetic agents required after pretreatment with clonidine. We recommend further studies to evaluate the effects of clonidine and anaesthetic agents together on respiration.

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Cardiovascular effects of intravenous clonidine

Partial attenuation of the pressor response to intubation by clonidine

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Summary

The effect of clonidine on the pressor and heart rate response to tracheal intubation was studied in a placebo-controlled, randomised, double-blind trial. Thirty patients were pretreated with either clonidine 1.25 μg/kg, or clonidine 0.625 μg/kg or an equivalent volume of normal saline, given intravenously 15 minutes before induction of anaesthesia. The attenuation of the pressor response to intubation of both clonidine groups was statistically significant compared to the saline group. Neither dose of clonidine completely abolished the increase in either heart rate or blood pressure. There was no difference in attenuation between the clonidine treatments; this indicated that the lower dose may be the more appropriate.

Key words

Intubation; tracheal.
Pharmacology; clonidine.

The haemodynamic responses to laryngoscopy and tracheal intubation, namely hypertension, arrhythmias and tachycardia, are of considerable importance to anaesthetists.[1,2] A variety of agents have been used to attenuate this response, including local anaesthetics,[3] opioids,[4] calcium channel blockers,[5] beta blockers[6,7] and vasodilators.[8] No single agent has been estabished as the most appropriate for this purpose. Clonidine, an alpha-2-adrenoceptor agonist, is an antihypertensive agent which decreases central sympathetic outflow thereby reducing blood pressure and heart rate.[9] Recent studies indicate that clonidine improves haemodynamic stability during cardiac surgery.[10] Oral clonidine has been shown to produce anxiolysis and sedation when administered as a premedicant.[11] While it may not be of use as a routine premedicant, it may be indicated where swings in blood pressure and heart rate might be potentially harmful.

The aim of this study is to examine the efficacy of two doses of intravenous clonidine, in decreasing the pressor and heart rate response to a standardised induction, laryngoscopy and tracheal intubation sequence.

Methods

This study was approved by the local Ethics Committee and informed consent was obtained from all patients.

Healthy ASA 1 subjects were premedicated with temazepam 20 mg administered orally 60–90 minutes before operation. Venous access was established and the patients were randomly allocated to one of three equal treatment groups: group A patients received clonidine 1.25 μg/kg, group B clonidine 0.625 μg/kg and group C an equivalent volume of normal saline. Each treatment was administered intravenously 15 minutes before induction of anaesthesia. Sedation was noted during this period.

Before administration of the test drug, a 22-gauge radial arterial cannula was sited using local anaesthesia. A Hewlett Packard monitor provided a continuous display of the arterial waveform, and a printout of blood pressure was produced at the set time intervals. Heart rate was measured using lead II of the ECG, and tissue oxygen saturation was monitored using a pulse oximeter.

Baseline values for heart rate and blood pressure were recorded before the administration of the test drug. Further readings were recorded at one-minute intervals for a 15-minute period before induction of anaesthesia, and from induction, heart rate and blood pressure were monitored and recorded at 1-minute intervals until 5 minutes after tracheal intubation.

Following three minutes of pre-oxygenation, anaesthesia was induced (to loss of verbal contact) with thiopentone 3–5 mg/kg and muscle relaxation produced by suxamethonium 1.5 mg/kg, both given intravenously. Direct laryngoscopy was performed 60 seconds later and tracheal intubation was completed within 15 seconds using a Macintosh laryngoscope. All intubations were performed

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Table 1. Demographic data of patients, mean (SEM).

	Control (saline)	Clonidine 0.625 μg/kg	Clonidine 1.25 μg/kg
Patients (*n*)	10	10	10
Male : female	4:6	6:4	4:6
Age; years	34 (4)	36 (4)	36 (3)
Weight; kg	59 (1)	65 (3)	69 (3)
Heart rate; beats/minute	80 (13)	72 (7)	75 (6)
MAP; mmHg	89 (2)	88 (7)	88 (4)
Thiopentone; mg/kg	5.4 (0.12)	4.6 (0.28)*	3.9 (0.26)*

* $p < 0.05$, compared to saline group.

by the first author who was unaware of the indentity of the test drug. Anaesthesia was maintained with 60% nitrous oxide in oxygen and 1% isoflurane, and vecuronium 0.1 mg/kg was administered intravenously 3 minutes after induction to allow ventilation. End-tidal carbon dioxide tension was maintained between 4.0 and 4.8 kPa.

Results are presented as mean (SEM). Statistical analysis was by repeated measures and two-way analysis of variance with range testing. Statistical significance was assumed at the 95% level ($p < 0.05$).

Results

Thirty patients were studied and formed three equal groups, which were comparable in respect of age, weight and gender, and in baseline values for mean arterial pressure (MAP) and heart rate, before test drug administration (Table 1).

Sedation before induction, as assessed by obvious drowsiness, was most marked in group A; 65% of patients were drowsy compared to 25% in group C. The dose of thiopentone required to produce loss response to verbal contact was significantly lower in groups A and B compared to group C (Table 1).

There were no statistically significant differences in the cardiovascular variables between the groups during the 15-minute period following injection of the test drug.

The changes in MAP and heart rate during laryngoscopy, tracheal intubation and for the 5-minute period thereafter are shown in Figures 1 and 2. Compared to baseline values, MAP decreased in groups A and B on induction of anaesthesia, and increased in group C (Fig. 1). In all three groups MAP increased significantly on laryngoscopy and intubation. In groups A and B, this increase from baseline was significant from intubation and lasted for 1 minute. The significant increase from baseline in

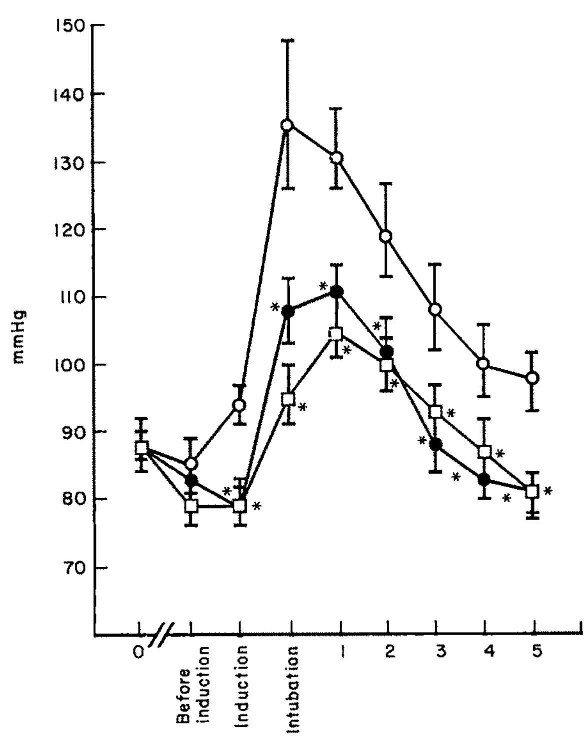

Fig. 1. Values for MAP from a baseline reading through induction and intubation, to a reading 5 minutes after intubation, mean (SEM). Clonidine 1.25 μg/kg, □; clonidine 0.625 μg/kg, ●; saline 0.9% 5 ml, ○. * $p < 0.05$ compared to saline group.

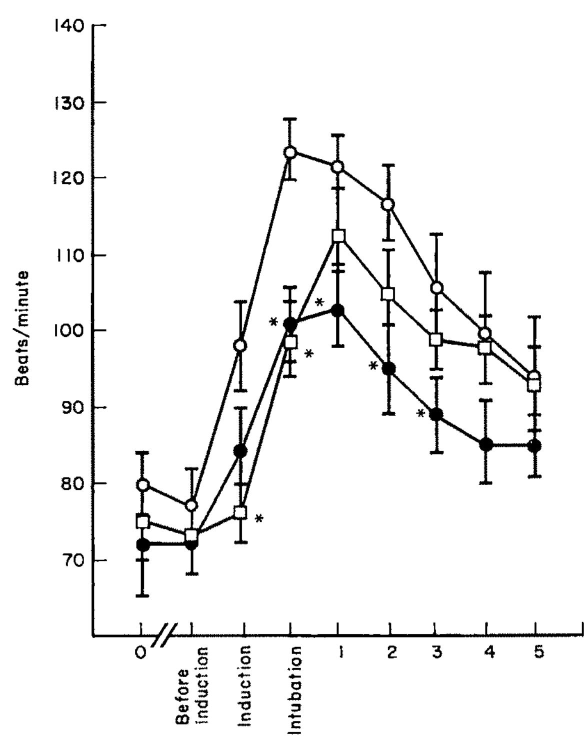

Fig. 2. Values for heart rate from a baseline reading through induction and intubation, to a reading 5 minutes after intubation, mean (SEM). Clonidine 1.25 μg/kg, □; clonidine 0.625 μg/kg, ●; saline 0.9% 5 ml, ○. * $p < 0.05$ compared to saline group.

group C persisted from intubation for 5 minutes. On between-group analysis, there was no significant differences between groups A and B following induction of anaesthesia. Compared to group C, MAP remained significantly lower in groups A and B from induction and intubation, continuing to 5 minutes after intubation. Thereafter there was no difference between the groups.

Compared to baseline values, heart rate increased after induction in all three groups and remained significantly elevated until 5 minutes after intubation (Fig. 2). On between-group analysis, significant differences were noted. In group A, the degree of tachycardia was significantly lower than in group C only at induction ($p < 0.01$) and intubation ($p < 0.05$), while in group B, the significantly lowered rate was noted from intubation for a 3-minute period ($p < 0.05$). There were no significant differences between groups A and B. One patient in group A developed a bradycardia of 45 beats/minute and a blood pressure of 75/50 mmHg, 5 minutes after the completion of the study. This responded to intravenous fluids and required no further treatment. No arrhythmias were observed in any patient in the three groups. There was no difference among the groups with respect to the incidence of nausea and vomiting.

Discussion

The haemodynamic changes associated with laryngoscopy and tracheal intubation can be marked, especially following thiopentone and suxamethonium induction. Stoelting reported that the arterial pressure increase began 15 seconds after laryngoscopy and achieved a maximum value after 30–45 seconds,[3] and MAP may increase by 50–70 mmHg, compared to a value before intubation.[12] While fit adults may tolerate these increases, such cardiovascular changes may be detrimental to patients with limited myocardial reserves. In the search for the ideal agent to attenuate these responses, a number have been advocated. Recently, the alpha-2-adrenergic agonists, which decrease central sympathetic outflow, have been the focus of attention for their potential stabilising effect on cardiovascular dynamics in the peri-operative period.[13] An increase in catecholamine levels has been noted during laryngoscopy,[14] and a more logical approach to the attenuation of such responses might be the reduction of sympathetic outflow. Clonidine is the only clinically available agent in the UK at present. In a recent editorial, Longnecker referred to marked haemodynamic responses in the peri-operative period as 'Alpine anesthesia', and suggested that clonidine may modify the valleys and peaks.[15] In this study, both doses of clonidine attenuated the blood pressure and heart rate responses after intubation when compared to an inert treatment group. The effect on MAP was similar in both the clonidine groups. Heart rate changes were more complex; the lower dose caused a more pronounced effect on heart rate.

This is difficult to explain, but other workers[16] have also noted a variable effect on heart rate with clonidine, which may be attributable to a baroreceptor response to changes in blood pressure, although this does not fully explain the findings of the study. However, despite the different duration of effect, both doses were associated with a weaker chronotropic response to intubation ($p < 0.01$) compared to the untreated group. These results are in agreement with previous work of Ghignone and coworkers[17] who noted that the haemodynamic responses to intubation were reduced in cardiac surgical patients who received oral clonidine in addition to routine premedication, and intra-operative cardiovascular stability was improved. This has also been confirmed by other workers.[18,19] On the other hand, it has been suggested that while clonidine may reduce MAP before induction and intubation, the subsequent pressor response is similar in treated and untreated patients.[20] In this study, the cardiovascular variables showed no statistically significant differences at the end of the 15-minute assessment period, and the maximum increase in MAP and heart rate noted in the clonidine groups was significantly lower than in the untreated groups. Intravenous clonidine may produce transient hypertension if administered rapidly, and although it lowers MAP, severe or postural hypotension are uncommon.[16] The maximim effect of intravenous clonidine occurs approximately 15 minutes after administration and is slow compared to other agents used for this purpose.

This study also supports previous findings[18] that the sedative effects of clonidine are dose dependent. Reduced inhalational anaesthetic requirements following the use of clonidine have been noted by previous workers[21] and our results suggest that this is true for thiopentone requirements and is a dose related phenomenon.

In conclusion, this study has demonstrated that clonidine partially attenuates the blood pressure and heart rate responses to tracheal intubation. The higher dose of clonidine offers no advantages over the lower dose, and may increase the risk of intra-operative hypotension. Although a low dose of clonidine may be useful in attenuating 'alpine anesthesia', and reducing anaesthetic requirements, the place of this drug in peri-operative management requires further assessment.

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A comparison of dopexamine and dopamine to prevent renal impairment in patients undergoing orthotopic liver transplantation

P. A. GRAY, A. R. BODENHAM AND G. R. PARK

Summary

The efficacy of low-dose dopamine as a renal protective agent was compared with that of dopexamine in patients who underwent orthotopic liver transplantation. Twelve patients who received a continuous infusion of dopexamine (1–3 μg/kg/minute) were matched for age, diagnosis, pre-operative creatinine clearance and blood loss with 12 patients who received a low-dose infusion of dopamine (2 μg/kg/minute). The catecholamine infusion was started after induction of anaesthesia and continued for 48 hours after surgery. Patients in the dopexamine group had less evidence of renal impairment and failure than those in the dopamine group during 7 days after the operation, although the differences between groups did not achieve statistical significance. Similarly there were no significant differences between the two groups in peri-operative urine output, urine/plasma osmolality ratio or creatinine clearance. Dopexamine is at least as effective as dopamine for renal protection in patients who undergo liver transplantation.

Key words

Surgery; liver transplantation.
Complications; kidney failure, acute.
Sympathetic nervous system, pharmacology; dopamine, dopexamine.

Patients who undergo orthotopic liver transplantation may suffer impaired renal function during the procedure or in the early postoperative period. The development of this complication is associated with a high mortality.[1] Major blood loss in the peri-operative period appears to be the most important factor which contributes to renal dysfunction. The resulting sympathetic vasoconstriction, which affects mainly the afferent glomerular arterioles, causes a decrease in renal blood flow and consequent renal ischaemia. Septicaemia and the use of potentially nephrotoxic drugs, such as cephalosporins or aminoglycoside antibiotics (especially in combination with loop diuretics) and the immunosuppressant cyclosporin A, may also be implicated.[2]

We suggested in a previous study[3] in liver transplant patients that the incidence of renal impairment could be reduced by the use of prophylactic low-dose dopamine (2.0 μg/kg/minute). Dopamine may exert a protective effect by reversing sympathetic vasoconstriction, or by maintaining or increasing renal blood flow and glomerular filtration rate.[4] However, 10% of patients treated with dopamine in that study developed renal failure. Other agents therefore need to be evaluated to see if this incidence can be reduced.

Dopexamine hydrochloride is a new synthetic catecholamine which stimulates dopaminergic receptors of the D_1 and D_2 subtypes with, respectively, about one-third and one-sixth the potency of dopamine.[5,6] Unlike dopamine, dopexamine also stimulates β_2-adrenoceptors, resulting in an additional increase in renal blood flow due to a direct effect on the renal vasculature.[7,8] There is no activity at α-adrenoceptors, and only minimal β_1-adrenoceptor activity.[5] Initial clinical experience[9] with dopexamine in the management of oliguria was encouraging and increased renal blood flow and urine output have been reported in patients with heart failure.[10,11] We decided to compare dopexamine with dopamine for renal protection in the peri-operative period in patients who underwent liver transplantation.

Methods

This open study involved two groups, each of 12 patients, who underwent orthotopic liver transplantation. Approval for the study was given by the District Ethics Committee and written informed consent was obtained from each patient. After induction of anaesthesia, a continuous intra-

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venous infusion of dopexamine at a rate of 2 μg/kg/minute was started in the first group. The infusion rate could be adjusted to 1 or 3 μg/kg/minute to achieve an increase in heart rate without exceeding an increase of 20 beats/minute, as a modest increase in heart rate is indicative of peripheral therapeutic effect. Similarly, systolic arterial pressure was not allowed to vary by more than 20 mmHg from the baseline value. The infusion of dopexamine was continued at this rate for 48 hours after the end of surgery, or until renal protection was no longer required.

Each patient was matched as far as possible for age, pre-operative creatinine clearance, blood loss and diagnosis with another patient who required liver transplantation. The matched patient received an infusion of dopamine (2 μg/kg/minute) from induction of anaesthesia until 48 hours after the end of surgery. The dose of dopamine was not varied because haemodynamic effects are unpredictable, unlike the dose-response relationship associated with the use of dopexamine. Furthermore, unnecessarily large doses of dopamine may increase renal vascular resistance, with a consequent deterioration in renal function. This does not occur with dopexamine.[12]

The anaesthetic and surgical techniques used in both groups have been described previously.[13,14] All patients received 10% mannitol 1 g/kg during the procedure. Prednisolone was administered for immunosuppression from the time of surgery and cyclosporin A was introduced approximately 3 days after operation after the initial effects of the surgical procedure had decreased.

Urine output was measured during the period of dissection, the anhepatic period, the period of biliary anastomosis, and hourly for 48 hours postoperatively in order to compare the efficacy of dopexamine and dopamine. The urine/plasma osmolality ratio was calculated pre-operatively, on admission to the intensive care unit (ICU) and on day 1 and day 2 postoperatively. Creatinine clearance was also measured pre-operatively and over the first and second 24-hour periods after operation. In addition, patients were observed for 7 days after operation to record the incidence of renal impairment or failure. Renal impairment was defined as oliguria (urine output less than 0.5 ml/kg/hour) in the presence of an adequate central venous pressure (> 10 mmHg) or pulmonary artery wedge pressure (> 12 mmHg) and a urine/plasma osmolality ratio of 1.1 or less, whilst renal failure was defined as the need for continuous haemofiltration with dialysis. The effects of the drugs on the splanchnic, peripheral and other circulations may differ because of their different adrenoceptor specificity; consequently, a note was made of the lowest systolic arterial pressure, and blood loss and replacement were recorded.

Frusemide, which is usually administered immediately before weaning from artificial ventilation,[15] was not given if the patient was polyuric or if weaning did not occur during the study period.

Student's *t*-tests for paired or unpaired data, the Mann–Whitney *U*-test, and Fisher's exact test were used for statistical analysis as appropriate.

Table 1. Details of patients in the two treatment groups. Data are expressed as mean (range).

	Dopexamine	Dopamine
Age; years	43.7 (24–56)	48.5 (24–58)
Gender; M : F	1 : 11	2 : 10
Weight; kg	58.4 (45.0–91.2)	58.1 (42.2–95.0)
Blood loss; litres	5.1 (1.5–15.0)	6.7 (1.4–12.0)
Blood replacement; litres	5.3 (1.5–14.7)	7.4 (1.0–16.5)
Lowest systolic arterial pressure; mmHg	69.2 (0–100)	70.0 (0–100)
Diagnosis		
Primary biliary cirrhosis	6	7
Chronic rejection	2	3
Neoplasm	3	0
Cryptogenic cirrhosis	1	1
Halothane hepatitis	0	1

Results

Demographic information is summarised in Table 1.

There were no statistically significant between-group differences in operative blood loss or its replacement, or in the lowest systolic arterial pressure recorded (Mann–Whitney *U*-test). Pre-operative urine/plasma osmolality ratios (before drug administration) were significantly greater in the dopexamine group than in the dopamine group ($p = 0.028$; Mann–Whitney *U*-test). There were no other significant differences between treatment groups during the infusion period (Mann–Whitney *U*-test). Creatinine clearance values did not differ significantly (Student's *t*-test for unpaired data). Urine volumes did not differ significantly either between the first and second 24-hour periods in each patient (Student's *t*-test for paired data) or between treatment groups (Student's *t*-test for unpaired data).

Five patients in the dopexamine group and nine in the dopamine group received frusemide but this difference was not statistically significant ($p = 0.1$, Fisher's exact test). The mean dose of frusemide administered was 32.9 mg in the dopexamine group and 43.3 mg in the dopamine group ($p = 0.078$, Mann–Whitney *U*-test).

The incidences of renal impairment and renal failure were greater in those patients who received dopamine than those who received dopexamine (Table 2) but these differences were not statistically significant (Fisher's exact test).

Table 2. Urine volumes, urine/plasma osmolality ratios, creatinine clearance values and incidence of renal dysfunction in the two treatment groups. Data are expressed as mean (SD).

	Dopexamine	Dopamine
Urine output; litres	$n = 11$	$n = 12$
0–24 hours	2.35 (0.45)	2.03 (0.80)
25–48 hours	2.21 (1.09)	2.21 (0.60)
Urine: plasma osmolality ratio	$n = 10$	$n = 6$
Pre-operative	2.1 (0.8)	1.5 (0.3)
Postoperative	1.4 (0.3)	1.3 (0.3)
Day 1 after surgery	2.0 (0.5)	1.6 (0.5)
Day 2 after surgery	2.3 (0.1)	2.1 (0.3)
Creatinine clearance (ml/minute)	$n = 9$	$n = 7$
Pre-operative	61.3 (24.1)	51.7 (12.4)
0–24 hours	57.6 (26.2)	58.6 (26.6)
24–48 hours	72.3 (40.5)	55.6 (40.5)

Discussion

Prevention of renal failure not only reduces mortality but also is more cost-effective, for example in terms of length of ICU stay and the need for haemodialysis. Dawson[16] demonstrated that the intra-operative administration of mannitol to jaundiced patients during surgery reduced the incidence of renal failure by promoting an osmotic diuresis. Similarly, dopaminergic agents may offer protection by maintaining or increasing renal blood flow, glomerular filtration rate and, hence, urine flow during periods when renal function might otherwise be at risk.

Infusions of dopamine in animals and humans increase renal blood flow[17] without significant changes in systemic arterial pressure.[18] The natriuresis and diuresis produced by dopamine may also involve intrarenal vascular changes[19,20] and alterations in the tubular transport of sodium[21] due to a direct effect on tubular D_1-receptors.[22] Dopamine may also inhibit vasopressin release.[23] In addition, an infusion of dopamine 4 μg/kg/minute was shown in dogs to ameliorate noradrenaline-induced vasoconstriction of the renal artery.[24] The dopamine precursor, γ-glutamyl dopa, has been shown to protect against glycerol-induced renal failure in rats;[25] similar results have been reported with dopexamine.[26]

Dopamine is a potent renal dopaminergic agonist if used in the dose range 2–5 μg/kg/minute and is used commonly to treat patients with incipient renal failure.[27] Low-dose dopamine has been reported to improve renal function in patients with renal failure due to cirrhosis[28] and during abdominal aortic aneurysm surgery.[29]

α-Adrenoceptor stimulation may provoke renal vasoconstriction and a decrease in renal blood flow. Dopamine is an α-adrenergic agonist at doses in excess of 10 μg/kg/minute although this effect has been observed even at low doses.[9] Dopamine may behave as a vasoconstrictor in the critically ill patient even at the relatively modest doses of up to 5 μg/kg/minute that are used typically for its renal effects (J. D. Edwards, personal communication). Dopexamine's lack of α-adrenoceptor activity[5] may thus be a potential advantage compared with dopamine. In addition, it is necessary to administer dopamine through a centrally placed venous catheter to avoid the risk of extravasation into the superficial tissues and subsequent skin necrosis due to intense α-adrenoceptor mediated vasoconstriction, whereas dopexamine can be infused safely through a peripheral vein.

Dopexamine possesses mild positive inotropic activity and may be useful when deterioration in renal function follows a decrease in cardiac output. The drug also produces generalised arterial vasodilation as a result of β_2-adrenoceptor stimulation and therefore potentially increases tissue perfusion in other organs, including the liver;[10,30] this may be advantageous in many clinical situations, especially in the critically ill.

The pharmacological profile of dopexamine suggests that it may be more effective clinically than dopamine for renal protection. However, we were able to identify only trends towards a lower incidence of renal impairment and failure in the dopexamine group, because of the small numbers of patients in the present study.

In an earlier study[3] the incidence of both renal impairment and failure was 9.5% in patients who received dopamine compared with 67% and 27% respectively in those who did not. In the present study, patients who received dopamine had a higher incidence of both renal impairment (66%) and failure (25%). There are three possible reasons for this difference. Firstly, children were included in the earlier study but were specifically excluded from this study. Children tolerate the major physiological insults of this and other operations better than adults, presumably because of lack of degenerative disease.

Secondly, in the 4 years which intervened between the studies, liver transplant operations have been extended to more seriously ill patients who are thus at greater risk of renal dysfunction, although the lack of severity scoring makes this difficult to substantiate. Finally, probably the most important difference was that the first study was retrospective while the present one was prospective. The retrospective design may have led to under-recognition of renal impairment. This argument is supported by the similar incidence of renal failure, which is more easily recognised, in the patients who received dopamine in the two studies.

The prophylactic use of dopexamine has been shown to be as effective as dopamine for renal protection in patients undergoing liver transplantation. Further prospective double-blind studies involving larger groups of patients are warranted.

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Plasma catecholamine response to cataract surgery: a comparison between general and local anaesthesia

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Summary

We studied the plasma catecholamine, plasma glucose and cardiovascular responses to cataract surgery in 20 elderly patients allocated randomly to receive either general anaesthesia or local anaesthesia by retrobulbar block. Local anaesthesia prevented the increase in plasma noradrenaline, adrenaline and glucose concentrations found in those patients who received general anaesthesia and also improved cardiovascular stability. The results show the beneficial effects of local anaesthesia in preventing the hormonal, metabolic and cardiovascular changes found when cataract surgery is conducted under general anaesthesia.

Key words

Anaesthetic techniques, regional; retrobulbar block.
Hormones; catecholamines.
Surgery; ophthalmological.

We showed in a previous study that local anaesthesia inhibited some of the endocrine and metabolic changes occurring in patients undergoing cataract surgery with general anaesthesia.[1] The metabolic response, as shown by changes in circulating glucose and lactate values, was relatively small and suggested only a limited increase in catecholamine secretion. The main object of the present study was to compare the plasma catecholamine response associated with cataract surgery in patients receiving either general or local anaesthesia. Concurrent changes in plasma glucose, arterial pressure and heart rate were also measured.

Methods

We studied 20 elderly patients admitted for cataract surgery. They were otherwise healthy and not receiving any medication known to interfere with the hormonal and metabolic response to surgery, and were suitable for either general anaesthesia (GA) or local anaesthesia (LA). The patients were allocated randomly to receive either GA or LA. The nature of the study was explained to them and informed consent obtained. The study was approved by the Hospital Ethics Committee.

No premedication was given to either group of patients. On arrival in the anaesthetic room a central venous catheter was inserted percutaneously via an antecubital fossa vein for collection of blood samples. A control blood sample was collected after a rest period of 10 minutes.

In the GA group anaesthesia was induced with a sleep-dose of thiopentone, the trachea intubated after the administration of vecuronium and the lungs ventilated with N_2O–O_2 and enflurane 0.6–1.0%. Ventilation was adjusted to maintain an end-tidal CO_2 tension above 4.0 kPa. Neuromuscular blockade was reversed with glycopyrronium 0.5 mg and neostigmine 2.5 mg on completion of surgery. In the LA group neural block was undertaken with a mixture of equal volumes of 2% lignocaine and 0.75% bupivacaine, without adrenaline. Three ml were injected as a retrobulbar block and 2 ml placed at the side of the eye to block the facial innervation of the orbicularis muscle. In both the GA and LA groups arterial pressure was measured noninvasively using a Datascope and the ECG and pulse oximetry were monitored continuously throughout the study.

In addition to the control blood sample, further venous blood was collected after induction of GA or LA, at the time of nuclear extraction, on completion of surgery, and 30 and 60 minutes after completion of surgery. The samples were centrifuged immediately and the supernatant stored at −20°C. Plasma for catecholamine determination was stored after the addition of 200 μlitre of an anti-oxidant

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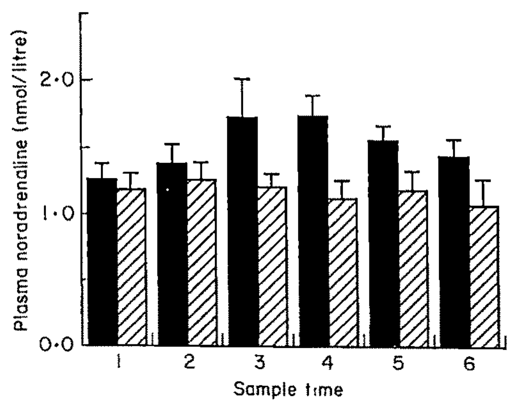

Fig. 1. Mean (SEM) plasma noradrenaline concentration (nmol/litre) in the GA group (solid bars) and LA group (hatched bars). Sample 1 before induction of anaesthesia, 2 after induction of anaesthesia, 3 at nuclear extraction, 4 at end of surgery, 5 at 30 minutes after completion of surgery, 6 at 60 minutes after completion of surgery.

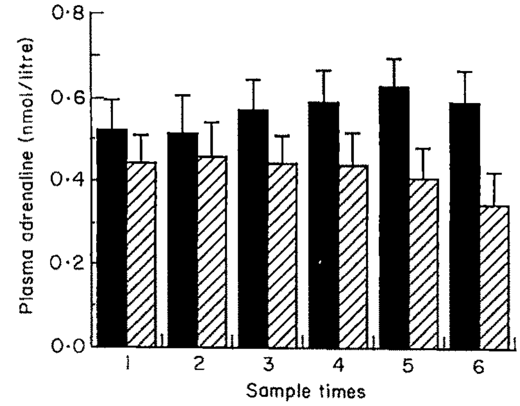

Fig. 2. Mean (SEM) plasma adrenaline concentration (nmol/litre) in the GA group (solid bars) and LA group (hatched bars). Sample times as for Figure 1.

solution (100 mmol/litre of reduced glutathione and 100 mmol/litre EGTA). Plasma glucose values were determined enzymatically as described previously.[2] Plasma noradrenaline and adrenaline concentrations were measured by HPLC with electrochemical detection.[3] The limits of detection of the assay were 0.1 nmol/litre for noradrenaline and 0.05 nmol/litre for adrenaline. The coefficients of variation for a pooled plasma sample (about 1.5 nmol/litre noradrenaline and 0.3 nmol/litre adrenaline) were 4.5% for noradrenaline and 8.2% for adrenaline.

The results are presented as mean values (SEM). Statistical analysis was undertaken using one-way analysis of variance, two-way analysis of variance and Fisher's exact test as appropriate.

Results

There was no significant difference between the groups with respect to age, body weight, sex distribution, time for induction of anaesthesia and duration of surgery (Table 1). The overall operating theatre time was significantly longer ($p < 0.05$) in the GA group (48 minutes GA group, 40 minutes LA group).

Plasma catecholamines (Figs 1 and 2). Plasma noradrenaline concentrations in the GA group increased from a control value of 1.25 nmol/litre to a peak value of 1.74 nmol/litre on completion of surgery. In the LA group, however, plasma noradrenaline varied little from the control value of 1.18 nmol/litre. Plasma noradrenaline values were significantly decreased in the LA group compared with the GA group at the end of surgery ($p < 0.01$), and at 30 and 60 minutes after completion of surgery ($p < 0.05$).

Plasma adrenaline values in the GA group increased from 0.52 nmol/litre in the control period to only 0.63 nmol/litre 30 minutes after completion of surgery. In the LA group plasma adrenaline concentrations were stable intra-operatively and then declined from a control value of 0.44 nmol/litre to 0.34 nmol/litre 60 minutes after completion of surgery. Plasma adrenaline values were significantly decreased in the LA group compared with the GA group at both 30 and 60 minutes after completion of surgery ($p < 0.05$).

Plasma glucose (Fig. 3). Plasma glucose increased intra-operatively and postoperatively in the GA group from 5.3 to 6.0 mmol/litre. There was little change in glucose values in the LA group with the result that there was a significant difference between the groups both during and after surgery ($p < 0.05$).

Mean arterial pressure and heart rate (Figs 4 and 5). Heart rate and mean arterial pressure were similar in both groups in the control period. Mean arterial pressure increased significantly in both groups after induction of anaesthesia, by 20 mmHg in the GA group ($p < 0.01$) and by 10 mmHg in the LA group ($p < 0.05$). In the GA group

Table 1. Details of patients studied. Mean values (SEM).

	LA group ($n = 10$)	GA group ($n = 10$)
Age; years	79.9 (1.5)	75.8 (4.5)
Weight; kg	57.9 (4.0)	62.7 (4.7)
Sex	2M:8F	1M:9F
Induction time; minutes	13 (0.9)	13 (1.2)
Duration of surgery; minutes	22 (1.3)	25 (1.9)
Start of induction to leaving operating theatre; minutes	40 (2.1)	48 (1.8)*

*Significant difference between mean values ($p < 0.05$).

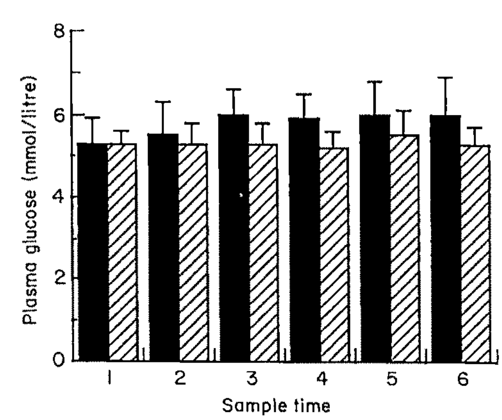

Fig. 3. Mean (SEM) plasma glucose concentration (mmol/litre) in the GA group (solid bars) and LA group (hatched bars). Sample times as for Figure 1.

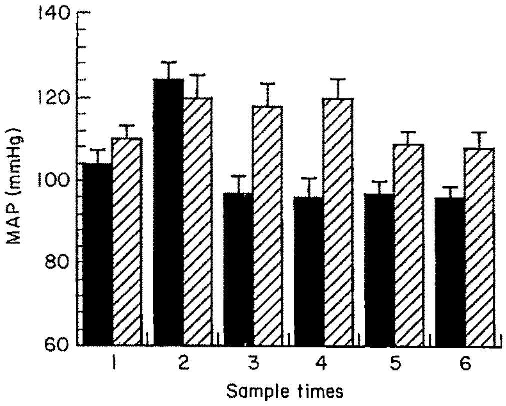

Fig. 4. Mean (SEM) arterial pressure (mmHg) in the GA group (solid bars) and LA group (hatched bars). Sample times as for Figure 1.

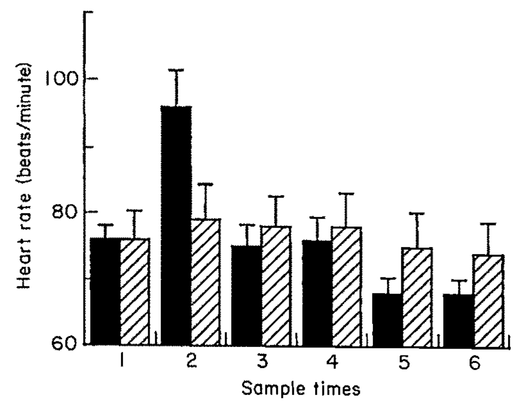

Fig. 5. Mean (SEM) heart rate (beats/minute) in the GA group (solid bars) and LA group (hatched bars). Sample times as for Figure 1.

arterial pressure decreased below control values during the rest of the study, whereas arterial pressure remained significantly higher ($p < 0.05$) throughout surgery in the LA group before declining to control values postoperatively. Arterial pressure was significantly higher in the LA group compared with the GA group at nuclear extraction, on completion of surgery and 30 minutes after completion of surgery ($p < 0.05$).

In contrast, heart rate varied little in the LA group throughout the study. In the GA group, however, there was a marked increase in heart rate after induction of anaesthesia from 76 to 96 beats/minute ($p < 0.01$), but this was not sustained during and after surgery. Heart rate was significantly higher in the GA group compared with the LA group only after induction of anaesthesia ($p < 0.01$).

Discussion

The results show clearly that LA prevented the increase in catecholamine secretion associated with cataract surgery under GA. The plasma noradrenaline and adrenaline values found in the control period were similar to those reported in unstressed, healthy individuals,[4] showing that the patients were comparatively stress-free in spite of the lack of premedication. Although increased sympathoadrenal activity during surgery mainly results from afferent stimuli from the operative site, it is also augmented by hypoxaemia, hypercarbia and blood loss. In the present study these physiological variables were comparable in the two groups, so that the abolition of sensory neuronal input from the eye in the LA group is likely to have been the cause of the difference in circulating catecholamines. The increases in plasma catecholamines in the GA group were only small (noradrenaline 0.49 nmol/litre, adrenaline 0.11 nmol/litre) and much less than those found in upper abdominal and pelvic surgery in which increases of up to 1.0 nmol/litre adrenaline have been observed.[5,6] This modest rise in sympathoadrenal activity is reflected in the small size of the glycaemic response, only 0.7 mmol/litre.

Local anaesthesia was associated with improved stability of arterial pressure and heart rate. Induction of GA resulted in the expected tachycardia and hypertension, since no attempt was made to obtund the response to laryngoscopy and intubation, but subsequently the arterial pressure was well controlled in the GA group. The significant increase in mean arterial pressure found after neural blockade in the LA group, which persisted for the intraoperative period, was only 10 mmHg and may have been caused by apprehension and fear. The changes in cardiovascular variables found at induction of anaesthesia in the GA group were not associated with a marked increase in circulating noradrenaline values. This discrepancy may be accounted for by the observation that circulating noradrenaline values probably only represent about 20% of the noradrenaline activity at the synapse and so grossly underestimate sympathetic nervous system activity.[7] A possible effect of thiopentone on decreasing tonic sympathetic activity may also have obtunded the noradrenaline response.[8] Previous studies have shown that general anaesthesia, *per se*, has little effect on the classical endocrine and metabolic response to surgery which results from surgical stimulation.[9]

The overall operating theatre time was significantly decreased in the LA group. This finding was in contrast to our previous study in which we failed to find any benefit in theatre utilisation.[1] It is notable that in the present study the duration of surgery was similar in the two groups, whereas previously it was significantly longer in the LA group. The results from both studies emphasise that the saving in overall time in the LA group occurs on completion of surgery and not on induction of anaesthesia.

In conclusion, we have shown that the plasma catecholamine and glucose responses to cataract surgery are abolished by LA and that this technique improves cardiovascular stability.

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CASE REPORT

Oral ketamine

Its use for mentally retarded adults requiring day care dental treatment

A. J. PETROS

Summary

Four cases of severely mentally handicapped young adults requiring day care dental treatment are reported. All had required varying degrees of restraint during previous dental treatments, which had been distressing for the patient, the relatives and the ward staff. In all cases, administration of oral ketamine 10 mg/kg, 30–60 minutes before the procedure, facilitated subsequent induction of anaesthesia.

Key words

Premedication; ketamine, oral.
Mental retardation.

Staff in day care dental units dealing with severely mentally handicapped young adults will be familiar with the problem of the physically fit, strong individual who reacts violently at the sight of a needle, since it is usually associated with sedative administration or induction of anaesthesia. Some of these patients are suspicious of all hospital staff and will simply not allow personal contact.

Case histories

Case 1

A 32-year-old educationally subnormal woman with Down's syndrome, weighing 61 kg, required two amalgam fillings. She had a mental age of a 6-year-old child and severely limited communication skills. She had had five previous dental treatments, in all of which she had required some degree of physical restraint to enable an intramuscular injection to be given. She was unsettled and totally uncooperative despite being accompanied by a foster parent. On this occasion she was offered ketamine orally and readily drank 15 ml of neat orange squash containing 600 mg ketamine hydrochloride. Thirty minutes later she was completely placid, but not unconscious. She allowed herself to be transferred onto the dental chair and permitted a gaseous induction of anaesthesia without any further problems. Although she was responsive within 10 minutes of stopping anaesthesia she took 4 hours to recover completely.

Case 2

A severely mentally handicapped 38-year-old woman, weighing 68 kg, required one amalgam filling. Her parents warned the staff that major difficulties had occurred during four previous general anaesthetics for dental treatment. She had a hysterical phobia for needles and would not allow strangers near her. She insisted on sitting in the corner of her room and attempts to approach or communicate with her resulted in further withdrawal and anxious, violent behaviour. She drank 700 mg of ketamine in orange squash, given to her by her parents, and was relaxed and approachable within 40 minutes. She took 6 hours to recover postoperatively.

Case 3

A 29-year-old autistic man, weighing 75 kg was accompanied by an attendant from the patient's institution. A previous attempt at dental examination had been unsuccessful and he had escaped from the ward despite physical restraint by a number of members of staff. On this occasion he was given 700 mg ketamine in 20 ml orange squash. He was manageable after one hour, although not completely placid. Intravenous access was secured and his teeth were scaled and polished. He took 6 hours to recover fully.

Case 4

A 16-year-old retarded boy weighing 51 kg who was unable to communicate required dental examination and one

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amalgam filling. He drank 500 mg ketamine and was sedated after 45 minutes. Venous access was secured without any difficulty, after which anaesthesia was induced. Recovery took 4 hours.

Discussion

Day care dental treatment for patients who are severely mentally handicapped can be a major problem. Treatment is frequently postponed or abandoned because anaesthesia cannot be provided. The alternative to day care, that of admission of the patient to a paediatric or psychiatric ward so that premedication can be given, does not solve the problem, but simply transfers it to the nursing staff on the ward. It is often more appropriate to treat these patients in the day care environment so that their degree of disorientation is minimised. Thus, the difficulty remains as to how to manage these patients. Trimeprazine is unsuitable as a premedication for adults. Oral benzodiazepines are inadequate and may not be swallowed. The application of EMLA (eutectic mixture of local anaesthetics) cream to reduce the pain of needle insertion is rarely successful. Intramuscular injections are often only achieved after combat and attempts at gaseous induction of anaesthesia can be disastrous.

In our day care unit the use of oral ketamine (Parke-Davies) in these extremely difficult cases has proved invaluable. It has been welcomed by the nursing staff and allowed one patient (case 3) who had previously been completely unapproachable, to be examined. The patients were happy to consume the camouflaged drug because they had all been fasted from midnight. Ketamine 8-10 mg/kg, mixed with neat orange squash to a volume of 15–20 ml and given one hour before surgery made all four patients cooperative within 60 minutes. It was then possible to establish intravenous access or perform a gaseous induction. After surgery, the patients recovered in a quiet, darkened environment, as is recommended after the use of ketamine. No emergence phenomena were observed.

There are an increasing number of reports of the use of oral ketamine. Its pharmacokinetics have been described in healthy volunteers.[1] Oral ketamine 0.5 mg/kg produced pain-free ischaemic exercise after 30 minutes compared with 15 minutes following intramuscular adminstration. After oral administration, absorption was found to be incomplete, with peak serum concentrations of approximately 20% of those obtained following the same intramuscular dose. Peak concentrations after oral administration occurred at 30 minutes, 8 minutes later than the intramuscular dose. Oral ketamine (1 mg/kg) has been used as an analgesic and was given one hour before the procedure in a 3-year-old girl who needed repeated changes of dressing for severe burns.[2] Less success was experienced with a 4-year-old with leukaemia who had had 20 previous anaesthetics.[3] However, a much higher dose of ketamine was used (12.5 mg/kg) and the patient complained of dizziness, had excess salivation and experienced 'emergence' phenomena. A single-blind study of 40 children with congenital heart disease,[4] compared premedication with oral trimeprazine 3 mg/kg and either intramuscular morphine 0.1 mg/kg or oral ketamine 10 mg/kg. The cardiovascular and respiratory effects and the degree of sedation induced was similar in both groups, suggesting that the use of oral ketamine was safe and effective. Oral ketamine 10–14 mg/kg was given as the sole agent in 30 children having extractions and conservative dental treatment[5] and its ease of use and strong analgesic properties were commended. A single case was described in which oral ketamine facilitated induction of anaesthesia in a combative mentally retarded patient who had a history of violent behaviour towards the medical staff.[6]

The oral administration of ketamine either as an analgesic or to induce anaesthesia is, therefore, a recognised technique. In a situation in which it may be hazardous for the staff to approach a patient or when the patient himself is distressed, the use of a small volume of attractive fluid containing ketamine may help to overcome the problem.

It has been found that the administration of small amounts of water before operation does not increase vomiting or significantly alter the pH of gastric contents and is associated with a decrease in residual gastric volume.[7] Ketamine has a pH of 3.5–5.5, and since it has a bitter taste, orange juice rather than water is required to disguise it.

Although the use of oral ketamine in children is not new, its administration to severely mentally retarded adults before dental anaesthesia deserves consideration. It should be noted, however, that full recovery of the patient may take 4–6 hours, so that appropriate facilities for care during this period must be available.

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Anaesthesia, 1991, Volume 46, pages 648–650

CASE REPORT

Spondyloepiphyseal dysplasia congenita

Caesarean section under epidural anaesthesia

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Summary

Spondyloepiphyseal dysplasia congenita is a rare condition with several features of concern to the anaesthetist. The patients are of extremely short stature and the presence of kyphoscoliosis may lead to significant respiratory impairment. Cervical vertebral body changes can result in spinal cord compression and laryngotracheal stenosis may be present. The management of such a patient presenting for elective Caesarean section under epidural anaesthesia is described.

Key words

Anaesthesia; obstetric.
Complications; spondyloepiphyseal dysplasia congenita.

Spondyloepiphyseal dysplasia congenita (SDC) is a rare disorder, which results in severely dwarfed patients with pathological changes involving primarily the vertebral column and the epiphyses of long bones. The condition is of particular concern to anaesthetists because of cervical spine instability and potential respiratory impairment.

The surgical management of complications resulting from this condition has been previously described.[1,2] However, there has only been one previous report on anaesthetic management (non-English language) and none which describe the particular problems encountered at Caesarean section.[3] In this paper we describe a case of SDC presenting for Caesarean section

Case history

A 23-year-old primigravid patient with SDC presented for Caesarean section. There was no past medical history of note apart from her congenital condition. She had not had any previous surgery and gave no history of neurological or respiratory problems. Anaesthetic advice had initially been sought at 18 weeks' gestation and an elective Caesarean section had been planned for 32 weeks' gestation, when it was considered that a compromise between fetal maturity and maternal respiratory impairment would have been reached. However, as there was no deterioration in maternal lung function at 32 weeks, the Caesarean section was delayed until 36 weeks.

On examination the patient was of strikingly short stature but had a normal facial appearance and unrestricted neck and jaw movement. Her height was 100 cm and weight 40 kg. Her limbs were essentially normal in length but her trunk was markedly shortened. The distance between symphysis pubis and xiphisternum measured only 20 cm, but because the gravid uterus had extended extra-abdominally, there was no respiratory impairment. The patient's back was grossly deformed, with a marked thoracic kyphoscoliosis and lumbar lordosis. There were no signs of neurological deficit.

Pre-operative investigations revealed normal lung function, full blood count, urea and electrolytes. Cervical spine X rays showed abnormal vertebral body configuration at all levels with a degree of subluxation at C_{3-4}. This movement was maximal in flexion (Fig. 1). There was no malalignment at C_1. In view of the cervical spine X ray changes it was decided to perform the Caesarean section under epidural anaesthesia.

The patient received 150 mg of ranitidine 12 and 2 hours pre-operatively and was given 30 ml of 0.3 M sodium citrate on arrival in the anaesthetic room. A 14-G intravenous cannula was then sited in a peripheral vein and an infusion of compound sodium lactate solution started. The epidural was performed with the patient in the sitting position. It was not possible to clearly define spinous processes at the lower lumbar level but an intervertebral gap was palpable at what was judged to be L_{1-2}. A 16-G Tuohy needle was introduced and using the loss of resistance to air technique, the epidural space was fairly easily entered at a depth of 2.5 cm from the skin. An epidural catheter was passed without difficulty but initially was found to be intravascular, as the

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Fig. 1. Cervical spine in flexion.

injection of 2 ml of 2% lignocaine with adrenaline 1:200000 caused a 50% increase in heart rate and a transient severe headache. The catheter was withdrawn until only 1 cm remained in the epidural space, at which point no further signs of intravascular placement occurred.

A total of 8 ml of 2% lignocaine with adrenaline 1:200000 was finally given into the epidural space; 2 ml sitting and 3 ml in both right and left lateral positions. Anaesthesia developed from the sacral segments to T_4 over a period of 25 minutes. Although 750 ml of compound sodium lactate solution had been infused intravenously during the onset of the block, a single dose of ephedrine 3 mg was necessary when the systolic blood pressure fell transiently from 120 to 90 mmHg. Thereafter, the course of the operation was uneventful. A 1970-g male infant was delivered with Apgar scores of nine at one minute and 10 at 5 minutes. After delivery pethidine 25 mg was given epidurally. The postoperative period was free of complications and the patient was discharged home 6 days later.

Discussion

SDC is a rare condition which results from either spontaneous genetic mutation or autosomal dominant inheritance. The condition is usually manifest from infancy when the characteristic physical and radiological changes become apparent. The spine is characterised by platyspondyly with central anterior pointing of the vertebral bodies. A point of particular concern to anaesthetists is odontoid hypoplasia which, combined with ligamentous laxity, leads to atlanto-occipital instability.[4] In this patient the most significant change in the cervical spine X ray was a degree of subluxation at the level of C_{3-4}. Computerised axial tomography of the spine may also be helpful in such patients, as myelographic studies have shown that the degree of cord compression does not always correlate with the radiographically measured instability.[1]

Thoracic dysplasia with respiratory failure has been described in SDC, which is of particular relevance if it is combined with the physiological changes of pregnancy. These include the reduction in functional residual capacity (FRC) due to diaphragmatic splinting by the gravid uterus, with increased shunting and reduced lung compliance. Although in our patient lung function tests did not show any reduction when compared with predicted values, it should be remembered that predicted values have been calculated for patients of similar weight and height, but normal physique. Despite this, our patient did not develop any overt respiratory impairment during or after her pregnancy. A further complication of this condition which can affect anaesthetic management is laryngotracheal stenosis, which has been described in more than one report.[2,3]

Additional anomalies may include myopia and retinal detachment. For this reason it is recommended that a full ophthalmological examination is carried out before surgery or anaesthesia. Finally, pectus cavinatum, cleft palate and talipes equino varus have been reported in association with SDC.[4]

The early involvement of the anaesthetic department in the assessment of this patient allowed sufficient time to arrange all necessary investigations and to formulate management plans for both elective and emergency procedures. Initially general anaesthesia was considered for this patient as it was thought that there would have been little difficulty in visualising the larynx. However, in view of the risks to the cervical spinal cord associated with head extension, and in particular the application of cricoid pressure precisely over those vertebrae shown to be most unstable, it was considered that a regional technique should be the first choice. Other potential problems, such as the possibility of laryngotracheal stenosis and an increased risk of aspiration and aortocaval compression favoured this decision. Fortunately this patient was keen to stay awake and as SDC infants do not look abnormal at birth, there was no contraindication to this.

A notable feature of this case was the unexpected ease with which the epidural space was entered. This was surprising in view of the marked kyphoscoliosis and the patient's diminutive stature. The shallow depth of the space (2.5 cm from skin) was predictable, but we were not certain that, having entered the space, it would then be easy to obtain adequate, uniform analgesia. However, a dense, bilateral block to T_4 was achieved in less than 30 minutes. The volume of local anaesthetic required (8 ml) was comparable to that described in other case reports of patients of pathologically short stature requiring Caesarean section.[5]

In conclusion, this case illustrates the need for early anaesthetic involvement with such patients. In particular, the risks of cervical spine instability should be of major concern when planning anaesthetic management. Furthermore, gravid patients are at a greater risk of both neurological and respiratory complications than nonpregnant patients. As this case demonstrates, a regional technique may be feasible in the presence of skeletal deformities, even if superficial examination of the patient's back suggests otherwise.

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CASE REPORT

Unilateral pulmonary oedema of the contralateral lung following transaxillary sympathectomy

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Summary

A previously healthy young male developed unilateral pulmonary oedema immediately after re-expansion of an intentionally collapsed lung after transaxillary sympathectomy. The pulmonary oedema was localised to the contralateral, uncollapsed lung.

Key words

Lung; oedema.
Surgery; sympathectomy.

Unilateral pulmonary oedema has been described as an unusual complication in a variety of clinical settings. The most widely reported are cases of so-called re-expansion pulmonary oedema following the treatment of pneumothorax[1] or relief of pleural effusion.[2] Upper airway obstruction,[3] pulmonary contusion,[4] prolonged positioning in the lateral decubitus position[5] and systemic-to-pulmonary artery shunt procedures[6] have also been associated with the development of unilateral pulmonary oedema.

These forms of unilateral pulmonary oedema occur usually on the ipsilateral side. More unusual is pulmonary oedema confined to the contralateral lung. We describe such a case following re-expansion of a collapsed lung in a previously healthy young male who had undergone a transaxillary sympathectomy. We propose a possible mechanism to explain the contralateral localisation of the pulmonary oedema.

Case history

A 25-year-old male was admitted to hospital for elective left transaxillary sympathectomy, because of causalgia affecting his left hand following a work accident. He had been previously well and, in particular, had no history of cardiac or pulmonary disease. Pre-anaesthetic assessment, including physical examination, blood count, electrolytes, electrocardiogram and chest X ray, was normal.

Anaesthesia was induced with intravenous thiopentone 3 mg/kg and fentanyl 0.2 mg, and maintained with nitrous oxide and oxygen (2:1 litres/minute). As the procedure is facilitated by collapse of the lung on the side of the operation, a right double-lumen tube was inserted and the left lung collapsed. The right lung was ventilated mechanically with lower tidal volumes (400 ml) and with increased frequency (16 breaths/minute). Neuromuscular blockade was maintained with atracurium. Monitoring included pulse oximetry and capnography. No increase in airway pressure, no decrease in oxygen saturation below 93%, and no episodes of haemodynamic instability were noted during anaesthesia. He received a total of 200 ml of saline 0.9% during the procedure, which lasted 20 minutes. The left lung was reinflated under direct vision after successful completion of the operation. An underwater seal chest drain was inserted and allowed to drain passively. Neuromuscular blockade was reversed by neostigmine 2.5 mg given with atropine 1 mg, and the double-lumen tube was removed. The patient was transferred to the recovery room, where he was noted to be awake and alert.

Shortly thereafter, he became tachypnoeic with a respiratory rate of 30 breaths/minute, developed a sinus tachycardia of 120 beats/minute and the oxygen saturation decreased to 68%. Examination revealed diffuse crepitations on the right side of the chest. The trachea was reintubated and intermittent positive pressure ventilation commenced. Frothy, blood-stained sputum was aspirated from the trachea. A chest X ray revealed right-sided

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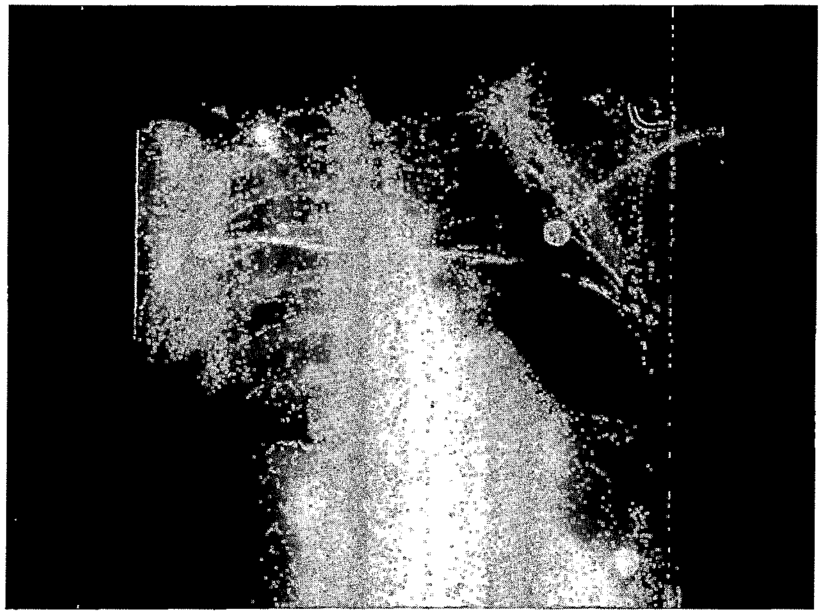

Fig. 1. Chest X ray immediately after re-expansion of the left lung, showing unilateral right-sided pulmonary oedema.

pulmonary oedema (Fig. 1). The left side of the chest was noted to be fully expanded. The patient was admitted to the intensive care unit where intermittent positive pressure ventilation was continued with an inspired oxygen concentration of 40%, respiratory rate of 10 breaths/minute, tidal volume of 750 ml and positive end-expiratory pressure (PEEP) of 0.6 kPa. Blood chemistry and blood count were normal and he was apyrexial. The central venous pressure (CVP) was found to be 5 cmH_2O. His condition improved rapidly and 2 hours after admission, arterial blood gas analysis showed an arterial oxygen tension of 20 kPa, oxygen saturation of 99%, arterial carbon dioxide tension of 4.2 kPa and a pH of 7.42. A repeat chest X ray 8 hours later (Fig. 2) showed significant clearing of the oedema fluid. The patient was weaned from the ventilator and the trachea extubated 12 hours after admission. He was transferred to a vascular surgery ward where he made an uneventful recovery and was discharged 4 days later. A chest X ray at that time was normal.

Discussion

We have described a patient who exhibited unilateral pulmonary oedema subsequent to re-expansion of a collapsed lung. The pulmonary oedema could conceivably have been due to other causes, such as excessive fluid loading or pulmonary aspiration. However, our patient received fluid replacement limited to match estimated losses, totalling 200 ml, and the CVP was 5 cmH_2O, making cardiogenic pulmonary oedema unlikely. The absence

Fig. 2. Chest X ray 8 hours after re-intubation, showing clearing of oedema.

of significant fever and leukocytosis, together with rapid clearing of the pulmonary infiltrate, argues against a diagnosis of aspirated gastric contents. Therefore, we believe that the pulmonary oedema in our patient was related directly to re-expansion of the collapsed lung.

Re-expansion pulmonary oedema, whether ipsilateral or contralateral, is thought to be the result of increased vascular permeability with consequent exudation of protein-rich fluid into the alveoli.[7,8] This altered permeability state may be the result of hypoxaemia[9] or decreased levels of surfactant,[10] or a consequence of the release of toxic metabolites following reperfusion of previously hypoxic tissue.[11]

The most interesting and unusual feature in this case is the fact that the pulmonary oedema was localised to the contralateral lung. Contralateral pulmonary oedema is a rarely described complication following re-expansion; in a recent review[12] of 59 cases of unilateral re-expansion pulmonary oedema related to pneumothorax, only three cases involved the contralateral lung. A prerequisite for the development of oedema of any organ is normal perfusion. Previous reports of contralateral pulmonary oedema are all associated with abnormal pulmonary vasculature of the nonoedematous lung.[10] These include absence or hypoplasia of a pulmonary artery, pulmonary thromboembolism, lobectomy, Swyer James syndrome and re-expansion of pneumothorax in patients with left heart failure. The patient we have described had, to our knowledge, normal pulmonary vessels but had undergone a transaxillary sympathectomy.

The importance of the sympathetic nervous system in altering lung permeability has received increasing attention. The pulmonary vasculature is innervated by both α- and β-fibres, with α-fibres predominating.[13] It appears that these fibres have a modulating effect on vasoconstrictive stimuli, such as hypoxia. Sympathetic discharge is thought to result in predominant venoconstriction, producing increases in pulmonary vascular resistance and hydrostatic pressure.[14] The result may be either a transudative, hydrostatic oedema or an exudative, haemorrhagic oedema due to microvascular rupture. Permeability may also be altered directly by sympathetically mediated contraction of endothelial cells, resulting in separation of these cells and transudation of fluid into the lung.[15] The contribution of the sympathetic nervous system is lent further credence by both experimental and clinical reports which suggest that interruption of sympathetic discharge may protect against the development of pulmonary oedema. Grauer *et al.*[16] have shown recently in an experimental model that prior denervation of a lung protected that lung, but not the innervated lung, from development of pulmonary oedema in dogs subjected to a period of increased intracranial pressure. In addition, chemical blockade with α-adrenergic blocking agents, such as chlorpromazine, has been shown to improve oxygenation following neurogenic pulmonary oedema.[17] A case of unilateral pulmonary oedema developed in a uraemic patient following a blood transfusion; the patient had undergone a thoracic sympathectomy 8 years previously and the pulmonary oedema occurred only in the lung contralateral to the sympathectomy.[18]

We believe that the sympathectomy that our patient had undergone protected that lung from the possible injurious consequences of lung collapse and re-expansion, namely hypoxia and reperfusion injury. The result was contralateral localisation of the oedema. This case lends further support to the importance of the autonomic nervous system in the production of re-expansion pulmonary oedema.

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CASE REPORT

Thoracic epidural analgesia in a patient with bilateral phaeochromocytoma undergoing coronary artery bypass grafting

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Summary

A patient suffering from phaeochromocytoma and coronary artery stenoses needed coronary artery bypass grafting before adrenalectomy. High thoracic epidural analgesia (T_1–T_2) with bupivacaine and sufentanil in combination with general anaesthesia was used. Plasma adrenaline and noradrenaline concentrations decreased during the period before bypass grafting compared to the baseline value and no important haemodynamic changes were seen during this period. Thoracic epidural analgesia failed to suppress the release of catecholamine during the bypass period. After the operation, the plasma catecholamine concentrations returned to the baseline value. Excellent analgesia (visual analogue scale = 1–2) was achieved with a postoperative epidural, but the plasma catecholamine concentration increased considerably.

Key words

Anaesthetic techniques, regional; epidural.
Surgery; phaeochromocytoma, cardiovascular.

In patients with phaeochromocytoma, producing adrenaline and noradrenaline, haemodynamic instability during adrenalectomy is frequent despite pretreatment with α- and β-blocking drugs. Release of catecholamines due to stress or manipulation of the adrenal glands causes hypertension and tachyarrythmias. In patients with angina at rest, the risk of myocardial infarction during adrenalectomy must be assumed to be high. A case is reported in which a patient with phaeochromocytoma and unstable angina (NYHA IV) underwent coronary artery bypass grafting, followed by adrenalectomy 6 weeks later.

Case history

A 73-year-old 85-kg man, height 184 cm, suffering from hypertension, coronary artery disease and hyperlipidaemia type IV, was admitted to hospital with unstable angina. Several times a week he suffered from periods of profuse sweating accompanied by headaches, dizziness and palpitations. The angina reduced and the ECG became normal with β-blocking drugs, nitrates and calcium antagonists. Further investigation revealed a high level of vanilyl mandelic acid (VMA) in the urine and a very high concentration of adrenaline and noradrenaline (1.1 nmol/litre and 4.7 nmol/litre) in plasma. The normal value for adrenaline is 0.06–0.30 nmol/litre and for noradrenaline 0.6–2.3 nmol/litre. MIBG- and CT-scan showed bilateral hyperplasia of the adrenal glands, and phaeochromocytoma was suspected. A low total circulating volume was found using the radioactive labelled erythrocytes method.

A 70% stenosis of the left anterior descending coronary artery (LAD), two consecutive segments of 80% stenosis of the circumflex coronary artery and a 75% stenosis of the right coronary artery (RCA) were demonstrated by coronary angiography. Ventriculography showed normal kinesis of the ventricular wall. The cardiac index was 3.4 litres/minute/sq m.

In view of the severe coronary artery pathology, the risk of myocardial infarction during adrenalectomy was considered to be high. For this reason it was decided to revascularise the myocardium first, followed by adrenalectomy 6 weeks later.

Anaesthetic management

One week before coronary artery bypass grafting (CABG), the patient was treated with α- and β-adrenoceptor blocking drugs (phenoxybenzamine and metoprolol), extra fluid and salt administration and a calcium antagonist (nifedipine). The day before surgery, the electrocardiogram showed regular sinus rhythm with right bundle branch block. The haemoglobin concentration was 9.5 mmol/litre; serum electrolytes, liver and kidney functions and the clotting studies were normal. There was no jugular venous distension.

An epidural catheter was inserted, 12 hours before

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Table 1. Times of sampling and measurements.

1.	Before induction = baseline value.
2.	Before tracheal intubation.
3.	Five minutes after tracheal intubation.
4.	Before skin incision.
5.	Five minutes after sternal spread.
6.	Before CPB.
7.	Five minutes after establishment of CPB.
8.	Five minutes after aortic cross clamping.
9.	At 30°C during CPB.
10.	At 28°C during CPB.
11.	During rewarming period.
12.	Aortic declamping.
13.	Fifteen minutes after termination of CPB.
14.	First postoperative day at 0800 hours.
15.	Second postoperative day at 0800 hours.
16.	Third postoperative day at 0800 hours.

surgery, at the T_1–T_2 level using the paramedian approach and hanging drop technique. On the day of surgery, the patient was premedicated with intramuscular midazolam 0.1 mg/kg 30 minutes before operation. At arrival in the operating theatre the left radial artery was cannulated and the arterial blood pressure was 120/85 mmHg at a heart rate of 73 beats/minute. After starting an intravenous drip and preloading with 500 ml Ringers lactate, an epidural bolus of 10 ml plain bupivacine 0.375% with sufentanil 1:200 000 (i.e. 5μg/ml) was administered. Anaesthesia was induced with etomidate 0.2 mg/kg, midazolam 0.1 mg/kg and sufentanil 0.5 μg/kg. Pancuronium 0.1 mg/kg was used to facilitate tracheal intubation. The lungs were ventilated with O_2:N_2O (FIO$_2$ 0.4) to maintain normocapnoea.

A triple lumen thermodilution pulmonary artery catheter was introduced via the right internal jugular vein. Anaesthesia was maintained with midazolam 0.1 mg/kg/hour and additional increments of pancuronium were administered when needed. A continuous epidural infusion of bupivacaine 0.125% with sufentanil 1:1000.000 (i.e. 1 μg/ml) was started after the initial bolus administration at an infusion rate of 10 ml/hour.

Before cardiopulmonary bypass (CPB) Ringers lactate or gelatine was given, if needed, to maintain ventricular filling and arterial blood pressures. Standard CPB with membrane oxygenator, nonpulsatile flow and haemodilution (haematocrit 20%–25%) was used at a flow rate of 1.5–2.2 litres/minute. The patient was cooled to 25°C and myocardial protection was achieved with 300 ml/minute of ice-cold cardioplegia solution and topical cooling of the heart. Heparin 2.5 mg/kg was administered just before the establishment of CPB.

The haemodynamic variables were recorded continuously and peripheral venous blood samples were collected for determination of adrenaline and noradrenaline. The times of sampling and measurements are listed in Table 1.

After completion of coronary artery bypass grafting (four saphenous vein grafts and left internal mammary artery graft) and rewarming, the patient was weaned from CPB using dopamine 4 μg/kg/minute after a total bypass time of 90 minutes. Following administration of protamine the activated clotting time returned to its value before operation.

The patient was transferred to the intensive care unit at the end of the procedure where epidural analgesia with bupivacaine 0.125% and sufentanil 1 μg/ml, 10 ml/hour, was continued until the fourth postoperative day. One hour after operation the patient was awake and breathing spontaneously. Two hours later resternotomy was performed because of excessive drainage from the pleural and mediastinal tubes (250 ml/hour). The same anaesthetic management (epidural analgesia in combination with general anaesthesia) was used for resternotomy. During the following intensive care period, dopamine 4–10 μg/kg was needed for 15 hours. The patient was extubated the next morning. Warfarin was started on the first and α- and β-blocking drugs on the third day after operation. On the fourth day after operation the epidural catheter was removed and minor analgesics were sufficient for pain relief. Ten days after surgery the patient was discharged from the hospital in good condition.

Six weeks later, bilateral adrenalectomy was performed. A similar anaesthetic technique was used and the epidural catheter was inserted at the T_8–T_9 level. Ten days after adrenalectomy, the patient was discharged well.

Results

The pretreatment with α- and β-blocking drugs, extra fluid and salt administration resulted in an increase in body weight to 88 kg. Normal erythrocyte and plasma volumes were also found after this pretreatment using the radioactive labelled erythrocyte method. The day before surgery, blood pressure (130/90 mmHg) and heart rate (78 beats/minute) were normal and the patient had no complaints of orthostatic hypotension.

After induction of anaesthesia, an expected decrease in blood pressure (28%), heart rate (16%) and plasma catecholamine concentrations were seen. No important haemodynamic changes were seen before CPB, except a slight increase (10%) in blood pressure and cardiac output after maximal sternal spread. The plasma catecholamine concentrations remained stable during this period (Table 2).

An increase in plasma catecholamine concentrations (adrenaline = 13.1 and noradrenaline = 19.7 nmol/litre) was seen after the establishment of CPB. However, there was no increase in systemic vascular resistance (Table 2).

ECG changes were not seen either during or after CPB periods. Despite excellent postoperative pain relief, plasma catecholamine concentrations increased to a very high level (highest concentration adrenaline 8.2 and noradrenaline 15.3 nmol/litre) in the second and third postoperative days without any deterioration in the haemodynamic variables (Table 2). No serious cardiac, pulmonary or neurological complications were seen. Postoperative ECG showed no significant changes compared with the pre-operative ECG.

During adrenalectomy 6 weeks later, periods of hypertension, tachycardia and very high plasma concentrations of catecholamines (highest concentration adrenaline 43.7 nml/litre and noradrenaline 50.3 nmol/litre) during manipulation of the adrenal glands were seen. Sodium nitroprusside and metoprolol were needed to treat hypertension and tachycardia. No cardiac complications were detected.

Discussion

Adrenalectomy in patients with phaeochromocytoma is often attended by periods of hypertension and tachycardia caused by release of catecholamines. In this case, the patient had a negative myocardial oxygen balance at rest, angina pectoris and ECG disturbances. Periods of hyper-

Table 2. Plasma catecholamine concentrations.

	Mean blood pressure; mmHg	Heart rate; beats/ minute	Central venous pressure; mmHg	Mean pulmonary artery pressure; mmHg	Pulmonary artery wedge pressure; mmHg	Cardiac output; litres/ minute	Perfusion flow; litres/ minute	Rectal temperature; °C	Adrenaline plasma concentration; nmol/litre	Noradrenaline plasma concentrations; nmol/litre	Systemic vascular resistance in dyne/second/cm^{-5}
1.*	97	73	—	—	—	—	—	—	2.9	7.2	—
2.	70	61	—	—	—	—	—	—	0.9	2.2	—
3.	76	60	—	—	—	—	—	—	0.7	1.5	—
4.	93	61	9	22	17	5.6	—	35.7	0.5	0.5	1200
5.	107	65	7	23	16	6.8	—	35.5	0.6	1.0	1176
6.	99	73	10	21	16	6.4	—	35.6	1.1	1.3	1113
7.	65	—	—	—	—	—	5.0	35.6	13.1	19.7	1040
8.	40	—	—	—	—	—	5.0	32.6	4.2	9.1	640
9.	42	—	—	—	—	—	5.0	31.1	4.9	11.7	672
10.	56	—	—	—	—	—	4.8	28.5	4.2	9.0	933
11.	73	—	—	—	—	—	4.7	28.0	2.8	3.8	1242
12.	63	—	—	—	—	—	5.0	32.7	7.0	14.0	1008
13.	81	88	8	24	13	6.4	—	36.0	2.3	4.2	913
14.	76	80	7	21	11	6.2	—	36.5	2.3	4.2	916
15.	88	90	7	20	9	5.8	—	37.3	8.2	15.3	1117
16.	81	95	7	19	8	6.0	—	37.8	6.3	12.1	987

* = measurement points (listed in Table 1).

tension and tachycardia may compromise myocardial oxygen balance and the risk of myocardial infarction is high. For this reason, it was decided to perform myocardial revascularisation first.

Patients with phaeochromocytoma have hypertension, high systemic vascular resistance and low circulating volume. To avoid severe hypotension after induction of anaesthesia (especially epidural anaesthesia)[1] due to peripheral vasodilatation, pretreatment with α-blocking drug and extra fluid and salt administration is necessary to restore the circulating volume. A β-blocking drug is added to this pretreatment to prevent (reflex) tachycardia.

Continuous epidural analgesia in combination with intra-operative intravenous anaesthesia was considered to be the method of choice for the following reasons. Firstly, partial blockade of sympathetic innervation of the heart (T_1–T_{4-5}) by high thoracic epidural analgesia will potentiate the effect of β-blocking drugs in preventing tachycardia.[2,3] Secondly, thoracic epidural blockade from T_1–T_{10} may decrease plasma catecholamine concentration in patients without phaeochromocytoma by partial blockade of sympathetic innervation of the adrenal glands and sufficient pain relief. Thirdly, the beneficial effects of high thoracic epidural analgesia on coronary artery circulation in patients with coronary artery stenoses has been described by many authors.[4–9]

It is, however, essential to insert the epidural catheter one day before surgery, to prevent the development of an epidural haematoma due to systemic heparinisation during CPB.[10,11] Sympathetic blockade of the heart can worsen left ventricular function, especially in patients with diskinesis of the left ventricle wall after operation.

To avoid moments of stress, it was decided to induce intravenous anaesthesia and epidural analgesia at the same time. Intravenous sufentanil 0.5 μg/kg was administered to prevent hypertension and tachycardia caused by tracheal intubation and leg incision. The addition of sufentanil to the bupivacaine solution was chosen to intensify the analgesia and to potentiate the duration of action of the local anaesthetic.[12] Sufentanil epidural analgesia has spinal and systemic effects.[13]

The systemic effects of sufentanil may contribute to the acceptance of the tracheal tube during the procedure. Bupivacaine 0.375% seems to be the most suitable concentration to obtain adequate analgesia without severe hypotension in patients with coronary artery disease.

After intravenous and epidural induction (Table 2, measurement point 2), arterial blood pressure, heart rate and the plasma catecholamine concentrations decreased below the baseline value. Tracheal intubation (Table 2, measurement point 3) did not change the haemodynamic variables or catecholamine concentrations. Just before skin incision (Table 2, measurement point 4), arterial blood pressure returned to the baseline value, while a further decrease in plasma catecholamine concentration was seen.

Sternal spread resulted in only a slight increase in arterial blood pressure, heart rate, cardiac output and the plasma catecholamine concentration compared with the values before skin incision (Table 2, measurement point 5 compared with measurement point 4).

During CPB, high plasma catecholamine concentrations are described by many authors using different anaesthetic methods.[14,15] Nonpulsatile flow, hypothermia, hypotension and haemodilution contribute to the increase in catecholamine plasma concentrations. In spite of adequate analgesia and partial blockade of the afferent nerve fibres to the adrenal glands, a large increase in plasma catecholamine concentrations was seen in this case at the establishment of CPB (Table 2, measurement point 7). Fortunately, high plasma catecholamine concentrations during this (CPB) period did not result in increase of myocardial oxygen consumption. The plasma catecholamine concentrations returned to the baseline value just after termination of CPB (Table 2, measurement point 13).

Postoperative analgesia and sedation are very important in patients with phaeochromocytoma. The excellent postoperative analgesia with continuous epidural infusion of bupivacaine and sufentanil seems to have contributed to postoperative haemodynamic stability and low plasma catecholamine concentrations on the first postoperative day (Table 2, measurement point 14). The high plasma catecholamine concentration on the second and third days (Table 2, measurement points 15 and 16) in spite of the excellent analgesia (visual analogue score = VAS: 1–2) was probably the result of reduced sedation.

In summary, thoracic epidural analgesia in combination with general anaesthesia seems to have been effective in preventing hypertension and tachycardia in a patient with phaeochromocytoma undergoing coronary artery surgery.

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CASE REPORT

The laryngeal mask airway

An unusual complication

A. C. MILLER AND P. BICKLER

Summary

The laryngeal mask airway is an important addition to the anaesthetist's armamentarium, but its use is not without the possibility for misfortune. We encountered an unusual and potentially serious complication. A patient's epiglottis became trapped between the pliable grates in the mask portion of the laryngeal mask and partially obstructed his airway. Should this problem occur and remain unnoticed, in addition to the problem of airway obstruction during the anaesthetic, the oedematous epiglottis could be severely injured upon removal of the laryngeal mask. This, in turn, could result in airway obstruction requiring emergency treatment.

Key words

Complications; airway obstruction.
Equipment; laryngeal mask.

The laryngeal mask airway is an effective alternative to tracheal intubation for some patients.[1–6] Moreover, in some cases the laryngeal mask has provided a secure airway for patients in whom tracheal intubation was difficult or impossible.[7–10] Although the use of this device is usually uneventful, we recently encountered an unusual and previously unreported complication.

Case history

A 28-year-old, 98 kg man presented for exploration of a hand wound and repair of lacerated nerves, ligaments, and muscles. His medical history included smoking and he had received an uncomplicated general anaesthetic 13 years before. Physical examination was normal except for mild expiratory wheezing. Premedication comprised two puffs each of metaproterenol and ipratropium from metered dose inhalers and 2 mg of midazolam intravenously. Anaesthesia was induced with isoflurane in 70% nitrous oxide plus 30% oxygen supplemented by intravenous fentanyl and thiopentone. Ventilation was spontaneous. The patient's airway was maintained easily after insertion of a nasopharyngeal airway. There was no indication for tracheal intubation, but the operation was expected to last several hours, so we used a laryngeal mask airway. This technique also avoided tracheal stimulation in a patient who had signs of increased airway reactivity. After a deep level of anaesthesia was achieved, a number four laryngeal mask (Intavent Ltd.) was inserted easily on the first attempt. A laryngoscope was not used. Correct position was confirmed by the detection of carbon dioxide in the end-tidal gases, by the auscultation of clear and equal breath sounds bilaterally, and by the observation of good chest and anaesthetic bag movement with spontaneous ventilation. Anaesthesia was maintained with isoflurane in 50 to 70% nitrous oxide with oxygen plus intravenous fentanyl. Shortly after the beginning of surgery, mild stridor and mild rocking motions of the chest and abdomen suggested partial airway obstruction. Neither placing the laryngeal mask slightly higher or lower in the hypopharynx nor altering the volume of air in the cuff improved the stridor or chest rocking. Similarly, adjusting the position of the head and neck did not relieve the obstruction. The end-tidal carbon dioxide concentration and oxyhaemoglobin saturation remained stable throughout the entire procedure at 6.67 to 6.80 kPa and 95–98%, respectively. A fibreoptic bronchoscope was inserted through a bronchoscope adaptor in the anaesthesia system and into the laryngeal mask airway. The patient's epiglottis was noted to have herniated through the rubber grates where the tube joins the mask portion of the airway (Figs 1 and 2). Mild oedema of the epiglottis and a few millilitres of blood were also observed. The laryngeal mask was removed while the patient was still deeply anaesthetised and laryngoscopy performed with a Macintosh number three blade. The epiglottis appeared normal except for the mild oedema; no lacerations were apparent. All other

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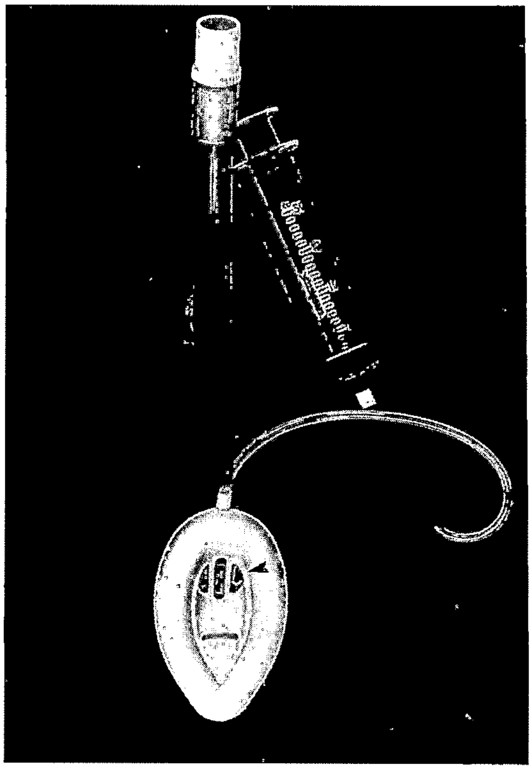

Fig. 1. Photograph of the laryngeal mask airway. Arrow indicates the pliable grates covering the opening where the tube and mask portions of the airway join.

laryngeal structures appeared normal. The patient recovered uneventfully. His postoperative course was unremarkable except for a moderately severe sore throat, which resolved.

Discussion

Although the laryngeal mask is generally easy to insert, it can occasionally be difficult to obtain a good fit. Assuming that the correct size laryngeal mask has been chosen, as recommended by Brain,[4] adjustments in head position, volume of air in the cuff, or depth of insertion in the hypopharynx are usually all that are necessary to achieve an excellent airway.[6] However, when repeated difficulty is encountered, especially if the patient's airway seems to be obstructed, the epiglottis is usually the problem. Several clinical series that tested prototype laryngeal masks reported that the epiglottis could become folded and obstruct the opening of the tube in the mask.[1-3]

The current version of the airway incorporates pliable grates over the opening of the tube in the mask to push the epiglottis away and prevent its obstructing the opening (Fig. 1). Folding of the epiglottis still occurs with the current commercial model, but airway obstruction does not necessarily occur.[9] Eight of 24 paediatric patients who underwent fibreoptic examination of the glottis while the present version of the laryngeal mask was in place exhibited folding of the epiglottis under the mask.[6] None demonstrated any signs of airway obstruction. However, as our case illustrates, the addition of the pliable grates has created the potential for a new problem. The patient's epiglottis can pass between the grates and partially obstruct the airway. Although the injury to the patient's

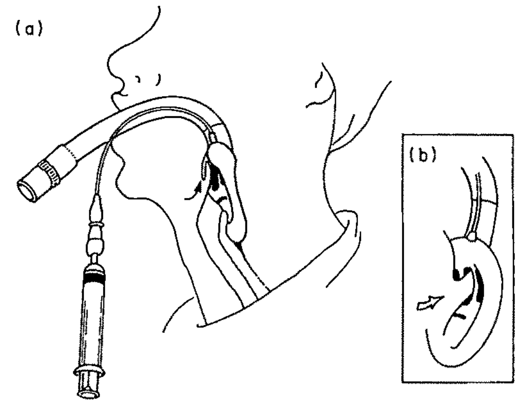

Fig. 2. (a) Illustration of the laryngeal mask airway in correct position. Arrow indicates the epiglottis in the proper location. (b) Illustration of the problem encountered in the case presented. The arrow indicates the herniation of the epiglottis through the grates in the mask.

epiglottis was mild in this instance, the potential for more serious injury exists, particularly in long cases where the epiglottis might swell and become lodged in the grates of the mask. In such a circumstance, in addition to the problems of airway obstruction during the anaesthetic, the epiglottis could become severely injured upon removal of the laryngeal mask. This, in turn, could result in airway obstruction requiring emergent treatment.

The laryngeal mask remains a significant addition to the anaesthetist's armamentarium for airway management. However, one must be aware of the potential for trapping the epiglottis in the mask and immediately investigate the cause of even mild obstruction to avoid this problem.

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CASE REPORT

Awake intubation: a new technique

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Summary

A 46-year-old male with a known history of difficult intubation presented for elective surgery. It was considered prudent to perform an awake intubation and a size 3 laryngeal mask was introduced under topical anaesthesia. A gum elastic bougie was then passed, enabling the laryngeal mask to be removed and a tracheal tube to be inserted.

Key words

Awake intubation; laryngeal mask.

The incidence of difficult intubation is unknown, but Rosen and Latto estimated it to be 1–3% of all intubations in anaesthetic practice.[1] In a known or suspected case of difficult intubation, particularly if there is risk of aspiration of gastric contents or problems with maintaining a patent airway, awake intubation should be considered. Several methods are available to assist the anaesthetist; these include blind nasal intubation and retrograde intubation techniques. The value of flexible fibreoptic instruments is well established,[2] but they are expensive, may not be available and require the operator to be experienced in their use to be effective.[3] We describe the use of the Brain laryngeal mask airway (LMA) as an aid to elective awake intubation.

Case history

A 46-year-old, 80 kg male presented for a series of semi-elective surgical procedures. Anaesthesia had previously been administered three times at another hospital and on each occasion intubation was attempted and found to be extremely difficult. The vocal cords were never visualised and intubation was eventually successful only after many attempts with a range of introducers in conjunction with a blind oral technique. The anaesthetists involved ranged in experience from a senior consultant to a junior registrar.

The fourth anaesthetic was administered by the authors and at the time neither the patient nor ourselves were aware of the problems previously experienced with intubation. Pre-anaesthetic assessment gave no clues that intubation might be difficult. The patient had reasonable neck movements, wide mouth opening and unremarkable dentition. Tracheal intubation was attempted after induction of anaesthesia and it proved impossible to visualise the vocal cords. The exact cause of the problem was unclear, but appeared to be related to an anteriorly placed larynx. It was possible to ventilate by mask, although it was difficult to maintain an adequate airway and on several occasions the peripheral oxygen saturation ($Sa\text{O}_2$) dropped to 85%. Intubation was eventually achieved using an introducer and a blind oral technique, but with considerable difficulty.

The patient's old notes were located after he recovered from surgery and the full history of difficult intubation was revealed. The patient was counselled about the difficulties experienced at intubation and provided with a 'medicalert' bracelet and a letter for the information of future anaesthetists involved with his care.

His fifth and final presentation was scheduled as a prolonged plastic surgical procedure. Intubation and ventilation was considered to be the anaesthetic technique of choice. It was thought prudent to perform an elective, awake intubation before induction because of the problems previously encountered. Informed consent was obtained and temazepam 20 mg was prescribed 1 hour before surgery as premedication.

Topical anaesthesia to the oropharynx was achieved with a gargle of 6 ml of 2% lignocaine. A laryngoscope was gently introduced over the tongue and 15-metered sprays of 10% lignocaine (10 mg lignocaine per spray) were applied to the laryngopharynx. Bilateral superior laryngeal nerve blocks were performed by cutaneous puncture at the level of the hyoid. Transtracheal injection of local anaesthetic was attempted but not tolerated by the patient.

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Fig. 1. The laryngeal mask and gum elastic bougie. Marks on the bougie are to aid orientation and indicate the position of the tip (see text).

Mild sedation was achieved with intravenous midazolam 2 mg. After pre-oxygenation, a well lubricated size 3 laryngeal mask airway (LMA) was introduced into the laryngopharynx. The cuff was inflated with 20 ml of air. The LMA was well tolerated and the patient breathed without difficulty. A gum elastic bougie (GEB) was inserted down the LMA and passed easily into the trachea. At this point the patient coughed, presumably due to tracheal irritation. The LMA was removed leaving the GEB in the trachea and a size 7.5 mm Portex tracheal tube was 'railroaded' down the GEB. General anaesthesia was then induced with propofol. The whole procedure of intubation had taken approximately 20 seconds and the patient maintained a good Sao_2 throughout.

There are several practical points relevant to this procedure. The tip of our GEB was curved up and forwards slightly to facilitate easy passage through the fenestrations in the LMA. Correct orientation of the GEB was ensured by reference to a vertical mark drawn anteriorly down the long axis of the bougie. A small horizontal mark identified when approximately 4 cm of the bougie had passed through the end of the LMA. The LMA could then be removed without dislodging the GEB from the trachea (Fig. 1).

When interviewed postoperatively, the patient stated that he had not found the awake intubation distressing and commented on the absence of a sore throat in contrast to previous anaesthetics.

Discussion

It is well recognised that the LMA may be used to guide into place a small tracheal tube and as such may be an aid to difficult intubation in the anaesthetised patient.[4–6] Use of the LMA to maintain a patent airway in cases of failed emergency intubation has also been well described by several authors.[5,7,8] Using an LMA as a guide to aid awake intubation has not, to our knowledge, been previously documented.

The LMA, although highly effective for airway maintenance, cannot always be considered a substitute for intubation. It does not necessarily form a complete seal around the larynx, and so does not provide complete protection against aspiration of gastric contents.[9,10] If high inflation pressures are required during IPPV, significant leaks are likely to occur.[5,11] In this case intubation was necessary to facilitate IPPV in the presence of known reduced lung compliance.

Passage of the LMA was well tolerated because of adequate topical anaesthesia and the soft compliant nature of the design. The method of topical anaesthesia employed was similar to that commonly used for other forms of awake intubation and no special manoeuvres were required. It is presumed that successful transtracheal injection of local anaesthetic would also have been helpful. Dasey and Mansour suggested that a successful superior laryngeal nerve block greatly reduced the incidence of coughing and/or laryngospasm with the LMA in anaesthetised patients.[12] It is reasonable to assume that good blockade of the superior laryngeal nerve is essential if the LMA is to be used as part of an awake intubation sequence.

Having successfully sited the LMA under topical anaesthesia, it is a relatively easy matter to pass a GEB through the lumen of the LMA into the trachea. Allison and McCrory were successful in the blind tracheal placement of a GEB using an LMA in the manner described in 21 out of 25 anaesthetised patients.[13] These authors found it necessary, as did we, to angulate the tip of the GEB anteriorly to ease its passage through the fenestrations in the LMA. They also marked the GEB in a similar manner to ourselves (see Fig. 1), to indicate the orientation of the angulated tip and the point at which it cleared the end of the LMA.

Awake intubation remains an important part of safe anaesthetic practice in many situations. Although flexible fibreoptic intubation is an extremely successful technique, it requires considerable expertise and is not applicable in all situations. It may be impossible after trauma to the oropharynx and nasopharynx where haemorrhage prevents adequate vision of airway structures.[14] Brain suggested that in cases where intubation was unusually difficult because of an anteriorly placed larynx, introduction of the LMA should be particularly easy.[5]

This case history illustrates that the combination of an LMA and GEB, placed under topical anaesthesia, can provide a simple method of performing an awake intubation.

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Anaesthesia, 1991, Volume 46, pages 664–667

APPARATUS

Use of the Inspiron nebuliser during continuous positive airway pressure ventilation

M. HARDWICK, G. DICKSON AND T. CLUTTON-BROCK

Summary

The Inspiron Nebuliser 002305 with air entrainment was assessed as a gas delivery device in a continuous positive airway pressure system. Inspired oxygen concentrations, total gas flows and pressures within the system were measured over a range of settings, with and without positive end expiratory pressure. Inspired oxygen concentrations and total flows were completely disrupted when a positive end expiratory pressure valve was applied, and the system failed to generate continuous positive airway pressure. We would not therefore recommend the Inspiron nebuliser as a gas delivery system for continuous positive airway pressure.

Key words

Equipment.
Ventilation; continuous positive airway pressure.

Continuous positive airway pressure (CPAP) ventilation has become a popular method of respiratory management in intubated, spontaneously ventilating patients, particularly as an aid to weaning.[1,2] It has been shown[3,4] that a number of systems which utilise the CPAP mode of a mechanical ventilator (i.e. a demand-valve system) cause an increase in the work of breathing. 'Home-made' continuous flow systems may be more effective in this respect, but problems arise in delivery of sufficiently high gas flows.

The Inspiron Nebuliser 002305 (CR Bard International) is an unheated nebuliser driven by oxygen with an adjustable Venturi entrainment device for air. At an oxygen flow of 10 litres per minute it delivers humidified oxygen over a range of inspired oxygen concentrations ($F\text{I}O_2$) between 0.35 and 1.0, with a total gas flow of up to 50 litres/minute[5] It is commonly used in hospitals for oxygen therapy in intubated and nonintubated, spontaneously breathing patients. For those patients who require a high $F\text{I}O_2$, two Inspirons in parallel may be needed to ensure an adequate gas flow.

At first sight it would appear that the Inspiron would make a suitable gas delivery system for CPAP, particularly since other Venturi devices have been shown to be effective.[6] We therefore conducted the following study to assess the Inspiron in a CPAP system.

Method

Oxygen at 10 litres/minute was supplied from a cylinder via a flowmeter to the inlet of the Inspiron. The outflow from the Inspiron was connected to a 2 m length of 22 mm corrugated disposable breathing hose, a previously calibrated oxygen analyser (Optotronic 74223) and then to a T-piece. The system pressures were monitored with a Deltran II (Utah Medical products) disposable pressure transducer and a Hewlett-Packard 78205 Amplifier, which had been calibrated against a mercury manometer at 0 and 20 mmHg. The expired gases passed via a No II Fleisch pneumotachograph connected to a Validyne DP45–16 differential pressure transducer and Gould 13–4615–35 carrier amplifier, to atmosphere or a disposable 0.5 kPa PEEP valve (Vital Signs Inc). The valve used has been shown to generate pressures that are reasonably flow-independent,[7] at the flows used in this study. The pneumotachograph was calibrated with air delivered from a GEC-Elliot 2000 rotameter, since Fisher[6] has shown that

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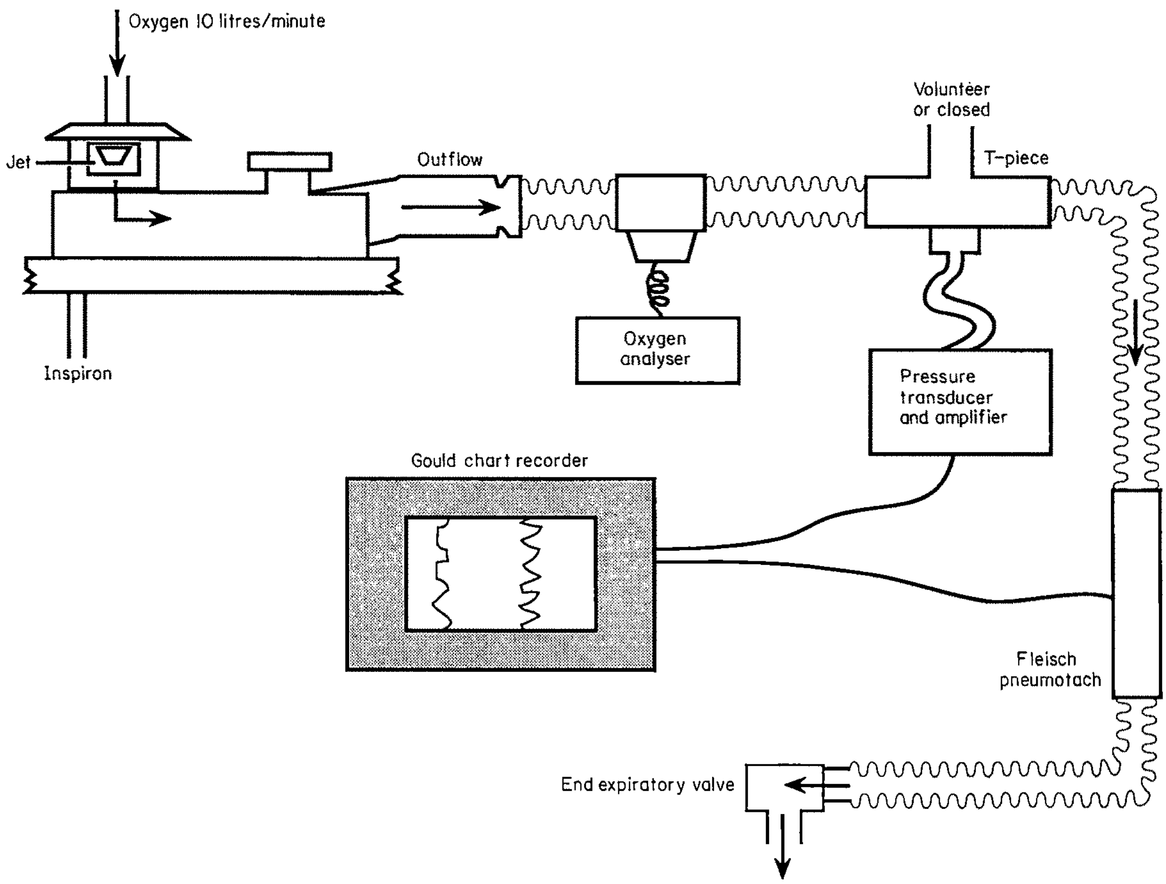

Fig. 1. System diagram.

altering the gas composition has only a small effect on the accuracy of the pneumotachograph. The Inspiron was used dry, since water vapour alters the viscosity of the gas and would affect the accuracy of the pneumotachograph; otherwise the conditions exactly mimicked those in practice. The outputs from the pressure and pneumotachograph amplifiers were recorded on a Gould RS 3400 Multichannel chart recorder. A system diagram is shown in Figure 1.

Recordings were taken with the Inspiron set at values of 35, 40, 50, 70 and 100% oxygen, under conditions of constant flow, with and without the 0.5 kPa PEEP valve, and then repeated during spontaneous ventilation provided by a healthy volunteer (M.H.) from a mouthpiece at the T-piece. All recordings were made when conditions had stabilised for one minute. The whole experiment was then repeated using two Inspirons in parallel, each driven by oxygen at a flow of 10 litres/minute.

Results

Figure 2 shows the accuracy of oxygen delivery of the Inspiron under different conditions. During continuous flow with no CPAP the measured $F\text{IO}_2$ agreed with the Inspiron setting, and although not illustrated, similar

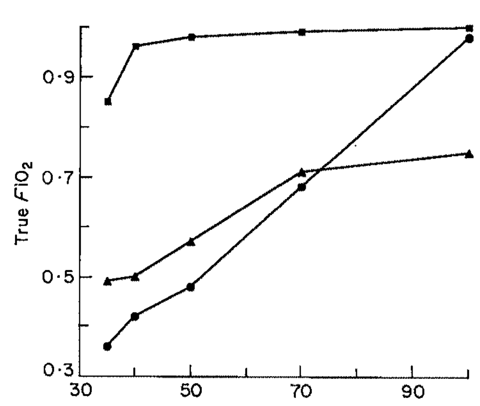

Fig. 2. Accuracy of oxygen delivery of a single Inspiron. ●, continuous flow without CPAP, ■, continuous flow with 0.5 kPa CPAP; ▲, spontaneous respiration with 0.5 kPa CPAP.

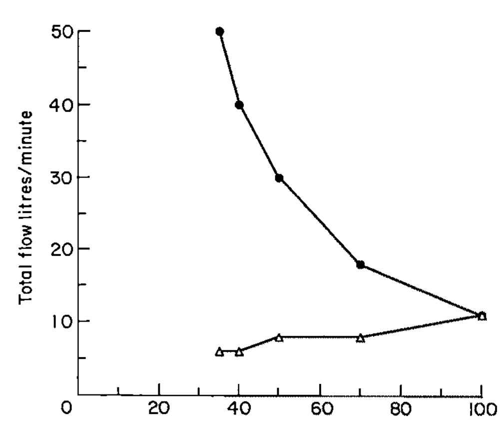

Fig. 3. Effect on total flow of adding 0.5 kPa CPAP to single Inspiron circuit. ●, continuous flow without CPAP; △, continuous flow with 0.5 kPa CPAP.

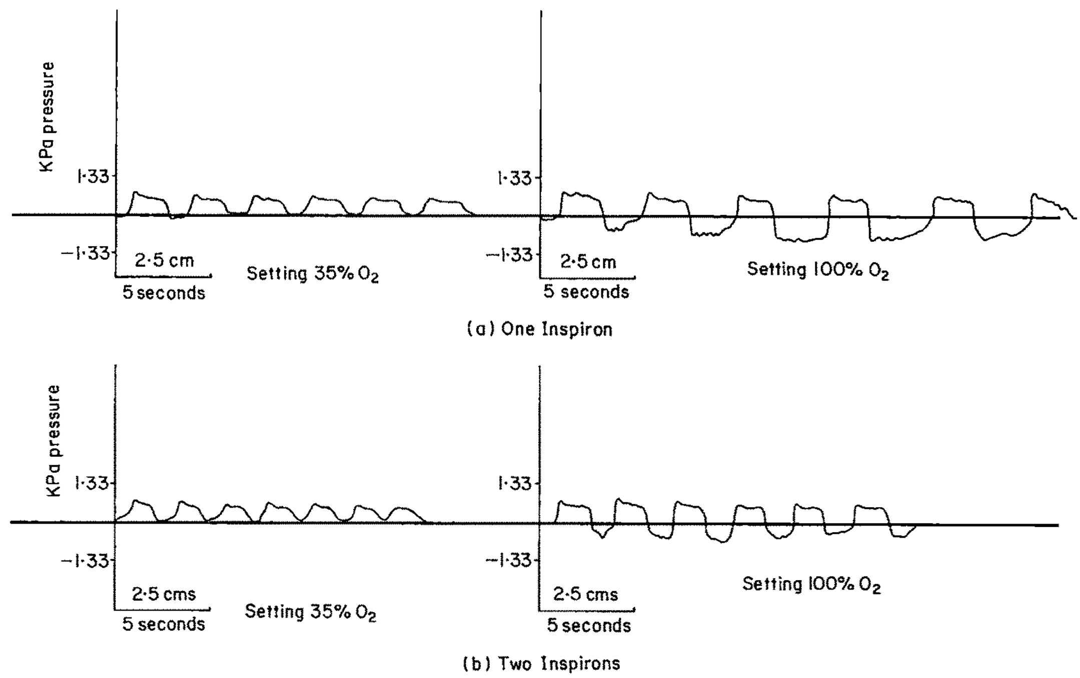

Fig. 4. Samples of pressure tracing produced during spontaneous ventilation with 0.5 kPa CPAP at two different oxygen settings; (a) using one Inspiron; (b) using two Inspirons in parallel.

results were obtained during spontaneous ventilation without CPAP. However, the addition of 0.5 kPa positive pressure caused the delivery of much higher oxygen concentrations during both continuous flow and spontaneous ventilation. The use of two Inspirons in parallel did not improve the performance of the system.

During constant flow without CPAP, the total flow delivered by the Inspiron decreased from 50 to 10 litres/minute as the oxygen setting on the device was increased (Fig. 3). When the 0.5 kPa valve was applied, the total flow was reduced at all settings and only reached a maximum of 10 litres/minute at an oxygen setting of 100%. Although the total flow of two parallel Inspirons was in excess of 50 litres/minute with no CPAP, when this was

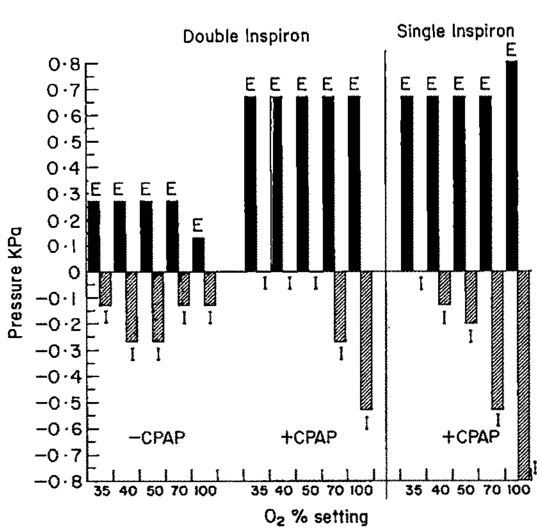

Fig. 5. System pressures generated during spontaneous ventilation under different conditions. E, end expiratory pressure; I, end inspiratory pressure.

added the total flow rate was again reduced at all settings and reached a maximum of 16.5 litres/minute at an oxygen setting of 100%.

Figure 4(a) is a sample of the pressure tracing produced during spontaneous ventilation by the volunteer through the system with the PEEP valve, with gas delivered by one Inspiron at settings of 35 and 100% oxygen. Figure 4(b) shows the pressure tracing under similar conditions, but using two parallel Inspirons at 35 and 100% oxygen settings. Using one Inspiron, the end-inspiratory pressure never attains a positive value, and reaches a negative value of 6 mmHg (0.8 kPa) at the higher oxygen settings. The results are similar using two parallel Inspirons.

Figure 5 shows the pressures generated in the system using two Inspirons over a range of settings, during spontaneous ventilation with and without CPAP. Positive pressures were only generated during expiration. Inspiratory pressures were zero or negative during spontaneous ventilation without CPAP. They became markedly negative during spontaneous ventilation with 0.5 kPa positive pressure at high oxygen settings i.e., when the Venturi aperture was small. With one Inspiron the results were similar but with greater negative pressures generated at high oxygen settings.

Discussion

The Inspiron humidifier with air entrainment is a convenient device for the delivery of humidified oxygen to spontaneously breathing patients under conditions of zero end-expiratory pressure.[5] Delivery of a high $F\text{IO}_2$ can be further guaranteed by the use of two parallel devices to increase total flow when air entrainment is low.

Disruption of the air entrainment characteristics of the device by the application of backpressure might be expected, and as we demonstrated, does occur to a marked extent. This not only produces lower than expected total

flows with elevated oxygen concentrations, but also fails to provide continuous positive airway pressures. When the total flow falls below the patient's inspiratory flow, the addition of the one-way PEEP valve prevents the patient from entraining air from the open end of the expiratory limb. This causes negative swings of pressure during inspiration. Less negative pressure is generated at low oxygen settings since it is possible to entrain air through the entrainment aperture under these conditions. Gherini[8] has shown that it is these swings in pressure that increase the work of breathing, a fact that was noted by the spontaneously breathing volunteer.

The documentation provided with the Inspiron 002305 is inadequate, as is noted by the health information document.[5] It makes no mention of the fact that addition of a PEEP valve into the system will dramatically reduce its total flow and fail to provide continuous positive airway pressure. The documentation does not provide adequate warning of the markedly elevated $F\text{IO}_2$ which may result, and its possible dangers for particular patients.

It is a very simple manoeuvre to attach a PEEP valve to the expiratory limb of an Inspiron system, and if equipment fittings are compatible (as they are in this case) there is no doubt that such a system will be used. However, because the interactions of a PEEP valve on the function of a Venturi device may be poorly understood, a situation is created that could be potentially harmful to the patient.

As a result of this study it is our opinion that the Inspiron Nebuliser 002305 should not be used as a gas delivery system in a CPAP system. Furthermore we would agree with others[6] that CPAP systems should not be assumed to be effective, or safe, unless used in conjunction with an oxygen analyser, an airway pressure monitor and a pressure relief valve.

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APPARATUS

Inaccuracy of pulse oximetry in patients with severe tricuspid regurgitation

K. G. STEWART AND S. J. ROWBOTTOM

Summary

The accuracy of pulse oximetry was studied in a group of patients with severe tricuspid regurgitation. Measurements of arterial oxygen saturation from a finger and an ear probe were compared with those from a radial arterial blood sample analysed in vitro. Lower values were obtained using the pulse oximeter; the difference ranged from +2% to −11%. The discrepancies between pulse oximeter and laboratory oximeter readings were greater in this group of patients than in a control group who did not have tricuspid regurgitation. There was, however, no correlation between the magnitude of this discrepancy and either the peak central venous pressure or the venous pulse pressure.

Key words

Monitoring; pulse oximetry.
Heart disease; tricuspid regurgitation.

The use of pulse oximetry has increased dramatically in recent years. Although the pulse oximeter is a valuable monitor, there are certain circumstances where the accuracy of pulse oximetry may decrease. Factors which are recognised as adversely affecting the pulse oximeter signal include the use of vasoconstrictors, hypothermia, hypotension, and the presence of abnormal haemoglobins.[1] A recent case report suggested that artefactually low readings of arterial oxygen saturation of haemoglobin ($Sa\text{o}_2$) may be obtained when the patient has pronounced jugular venous pulsations.[2] We have studied the reliability of pulse oximetry in a group of patients with prominent retrograde jugular venous pulsations due to documented regurgitation of the tricuspid valve.

Methods

Two groups of patients were investigated. The study group consisted of 22 adult Chinese patients who were scheduled to undergo open heart surgery. All had chronic rheumatic heart disease and at cardiac catheterisation had been shown to have severe tricuspid regurgitation to a degree that tricuspid annuloplasty was planned as part of the operative procedure.

A radial artery cannula was inserted before surgery. The patient was then left undisturbed breathing room air for 5 minutes. After this $Sa\text{o}_2$ was measured using both finger and ear probes from an Ohmeda Biox 3700 pulse oximeter. Values were only recorded when the reading was stable and no error messages were indicated on the display screen. Simultaneously, an arterial blood sample was withdrawn. The $Sa\text{o}_2$ was measured without delay on a laboratory oximeter (Osm 2 Hemoximeter, Radiometer, Copenhagen) which had recently been calibrated according to the manufacturer's instructions. The systolic venous pressure (equivalent to the enhanced jugular 'V' wave), and venous pulse pressure, measured via an internal jugular cannula, were also recorded.

As a comparison, a control group of 20 patients who did not have tricuspid regurgitation, but were undergoing surgery for coronary artery disease or pulmonary neoplasia, were studied in a similar fashion over the same period of time. Central venous pressure measurements were not available for this group of patients.

Statistical analysis was by Wilcoxon signed rank test to analyse within-group discrepancies between laboratory and pulse oximeter results. The Mann-Whitney U test was used to compare the magnitude of these discrepancies in each group, and Spearman's rank correlation was used to determine any relationship between either peak central venous pressure (CVP) or venous pulse pressure and the results of the oximetry measurements.

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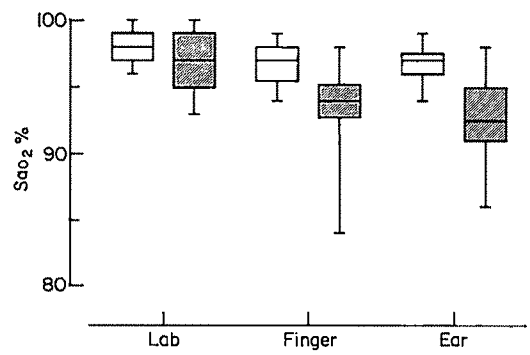

Fig. 1. Values of Sao_2 obtained by *in vitro* oximetry (lab) and from the two pulse oximeter probe sites. Median, interquartile, and range values are displayed. □, control; ▨, tricuspid regurgitation. For details of statistical significance, see text.

Results

The values of arterial oxygen saturation of haemoglobin obtained using the different measuring techniques and probe sites are demonstrated in Figure 1. In each group the laboratory oximeter registered higher values ($p < 0.01$) for Sao_2 than the pulse oximeter's finger and ear probes. In the control group the discrepancies between results obtained by *in vitro* measurement and those displayed on the pulse oximeter were smaller. In this group, the median (range) difference between laboratory oximeter and ear pulse oximetry was 1% (0 to +4%), compared with 4% (0 to +11%) in the study group. Similarly, in the control group, laboratory oximetry measurements exceeded finger pulse oximetry values by only 1% (−1 to +5%) compared with 3% (−2 to +10%) in those with tricuspid regurgitation. For both probe sites, the discrepancy between pulse oximeter and *in vitro* values was significantly greater in the study group ($0.01 < p < 0.05$).

Values obtained from the different pulse oximeter probe sites were compared. In the study group the finger probe gave statistically higher readings ($0.01 < p < 0.05$) than the ear probe by a median value of 1% (range −2 to +7%), although there was no difference between these values in the control group.

Satisfactory CVP recordings were obtained from 19 patients with tricuspid regurgitation. Peak systolic venous pressure measurements ranged from 8 to 40 mmHg. Neither this pressure nor the venous pulse pressure (difference between systolic and diastolic venous pressure) correlated with the degree of desaturation as measured by the laboratory oximeter. Similarly, there was no relationship between either peak venous pressure or venous pulse pressure and the magnitude of the discrepancy between values of Sao_2 obtained using the laboratory oximeter and pulse oximetry at either probe site (Figs 2 and 3).

Discussion

The principles upon which pulse oximeters depend are described elsewhere.[3] The assumption that all pulsatile flow is arterial allows calculation of Sao_2. In the case of patients who have prominent venous pulsations, this assumption may lead to inaccuracy, with venous interference causing an underestimation of the Sao_2. Mark[2] reported this problem with two patients, one of whom had

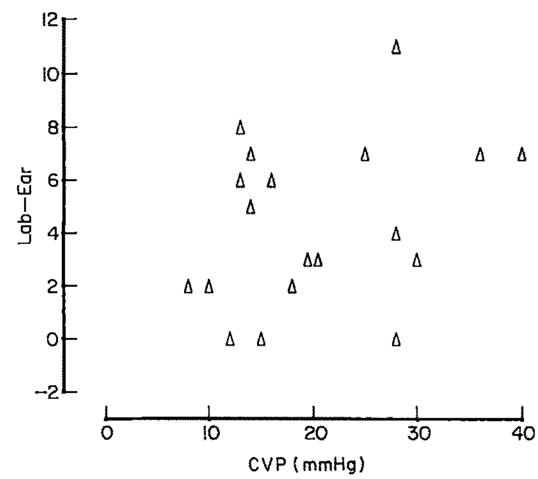

Fig. 2. Plot of peak CVP measurement against discrepancy between values of Sao_2 obtained *in vitro* (lab) and those displayed on the pulse oximeter using the ear probe.

tricuspid regurgitation; the other had increased venous pulsations secondary to ischaemic heart disease.

A similar problem has been described when a nasal pulse oximeter probe was used in a patient who required high airway pressures to enable mechanical ventilation.[4] The waveform obtained had a rate equivalent to that of the ventilator with falsely low Sao_2 values displayed. It was suggested that phasic venous congestion from high airway pressures had been detected by the pulse oximeter. In another study, lower Sao_2 readings were demonstrated when venous congestion was induced by placing the probe site in a dependent position.[5] The authors concluded that pulse oximeters normally sense venous pulsations, transmitted from arterial pulsations via arterio-venous anastomoses.

A control group was included in the present study in order to validate the equipment which we were using. The patients in the control group were older and heavier than those in the study group. This was to be expected due to the natural history of rheumatic heart disease, and these factors should not influence pulse oximeter readings. Previous studies have demonstrated good correlation

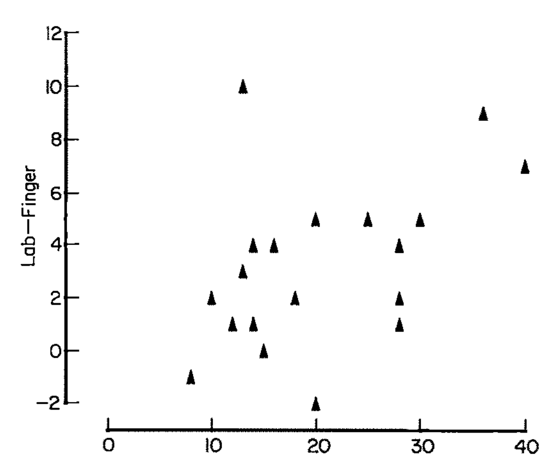

Fig. 3. Plot of peak CVP measurement against discrepancy between values of Sao_2 obtained *in vitro* (lab) and those displayed on the pulse oximeter using the finger probe.

between *in vitro* and pulse oximetry results,[6] as was the case in this study. In only three patients from the control group did the laboratory oximeter result exceed either pulse oximeter reading by greater than 2%.

Two probe sites were used since the finger probe could be more accurate than the ear probe in patients with tricuspid regurgitation. Greater attenuation of the retrograde pulsations is likely at the more peripheral site due to distance from the central veins and the presence of venous valves. Overall, the finger was a more reliable probe position in the study group. However, there were instances where large discrepancies occurred and in six cases the finger probe recording was less than the ear.

Although large discrepancies between pulse oximeter and laboratory oximeter readings occurred in several cases where peak venous pressure measurements were high, this was not always the case. There was no correlation between the degree of venous hypertension and the magnitude of the discrepancy, so venous pressure was a poor predictor of the accuracy of pulse oximetry. Similarly, using venous pulse pressure (the difference between venous systolic and diastolic values) as a comparison did not help us to predict the occurrence of large discrepancies between *in vitro* and pulse oximetry results. This finding is not unexpected since several other factors, such as venous oxygen saturation of haemoglobin and the synchrony of the venous with the arterial wave, may interact to determine the degree of interference.

In conclusion, using this model of pulse oximeter, we have demonstrated that the displayed reading of Sa_{O_2} may underestimate the true value in patients who have severe tricuspid regurgitation. It is difficult to predict the degree of interference likely for any individual patient. We recommend caution in interpreting the information obtained by pulse oximetry in such patients.

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APPARATUS

Faulty Superset plastic catheter mounts

A cautionary tale applicable to other mass-produced disposable products

J. G. HANNINGTON-KIFF

Summary

Nine Superset (Intersurgical Ltd) single-use corrugated plastic catheter mounts were found to be faulty in a boxed batch of 75. The manufacturer's meticulous system of batch coding enabled the source of the problem to be traced quickly. Sporadic faults must be expected to occur in mass-produced disposable equipment and the unusual origin of the defect reported in these catheter mounts is testimony to the way unexpected events can prejudice the most carefully regulated quality control. It is emphasised that the user can help safeguard the community by ensuring that stock is used in strict rotation and that batch numbers are accurately reported when faults arise.

Key words

Equipment; catheter mounts.

Events leading to a critical incident are always instructive but occasionally the interplay of some entirely unforeseen factors makes them all the more fascinating. The background to this account of a potentially perilous moment during a routine anaesthetic procedure, when an unexpected fault was encountered in a component part of the breathing system, reads like a kind of clinical Cluedo. These are the clues to contemplate: an idea forms in a McDonald's Golden Arch Restaurant, the idea materialises in a factory situated in a balmy Channel Island, a sample of the product causes concern during surgery in a Surrey Clinic, the solution lies in the involvement of a chilly Midland border town renowned for its second-hand book shops, and the tale ends happily with lessons learned and nobody hurt.

The critical incident

It became evident at an early stage of a hysterectomy under general anaesthesia that there was a leak in the breathing system through which some of the gas was being lost during the positive pressure phase of the mechanical ventilation of the patient's lungs. The anaesthetic machine and breathing system had been used on the previous two patients on the operating list without problem and the cuff on the tracheal tube was adequately inflated, so the fault probably lay in the disposable plastic catheter mount (trade name Superset, manufactured by Intersurgical Ltd). It is common practice nowadays to use sterile, disposable plastic tracheal tubes and catheter mounts (the flexible coupling which connects the breathing system to the tracheal tube) to minimise cross infection between patients.

Close examination of the catheter mount showed that there was a split at the bottom of the corrugation nearest the 15-mm male connector that couples with the breathing system (Fig. 1). The split only became obvious if the male connector was displaced to one side (Fig. 2). The defective catheter mount had been taken from a newly opened box containing 75 and it was found that altogether nine (12%) were split at the same site. Accordingly, the manufacturer was contacted and given the batch number. It was understood from the manufacturer that the factory rejection rate was normally less than 1% so what had gone wrong?

The Superset catheter mount

The designer of the Superset catheter mount was inspired by the sight of his small children drinking milk shakes through those ingenious straws with a corrugated section which can be set at different angles. He realised that an anaesthetic catheter mount with folding and setting corrugations would not only provide flexibility but allow the internal deadspace to be kept to a minimum. The Superset catheter mount has a deadspace of 25 ml when closed to its shortest length of 45 mm and only increases to 60 ml when fully stretched to 125 mm, as might be needed when it is bent through 180 degrees.

The device is made in one piece (except for the angulated connector which is added later), beginning with injection moulding of the 15-mm diameter male connector, followed

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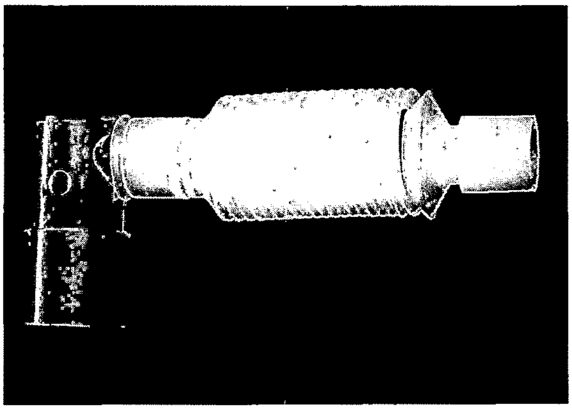

Fig. 1. Superset catheter mount showing split corrugation.

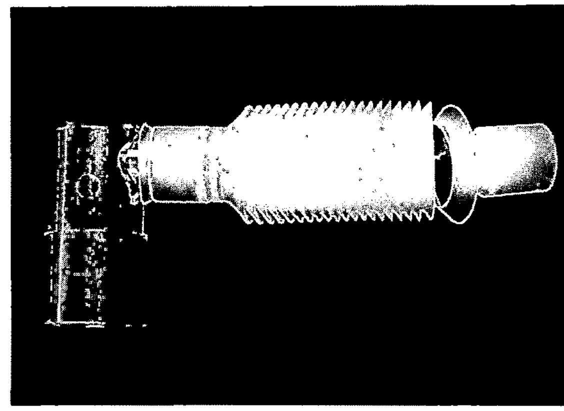

Fig. 2. Split forced open to show over-stressed plastic (opaque-white) at the broken edges of the ruptured corrugation.

by extrusion of a tube which is subsequently blown from the inside into a surrounding clamp mould to form the corrugations. The whole must then be left to rest for several days to allow the plastic to develop the required structural characteristics. The corrugations are then folded and unfolded by hand in a concertina action so that the tops and bottoms of the corrugations become overstressed, forming surprisingly robust 'clicking' hinges which confer the 'setting' property. The translucent plastic becomes white and opaque in the overstressed locations (Fig. 2).

It is crucial that the corrugations are manipulated at an ambient temperature above 18°C otherwise the normally strong overstressed edges of the corrugations may split. Herein lies the clue to what probably happened to the defective batch. The catheter mounts are normally finished in the Guernsey factory where it is easy to maintain the ambient temperature above 18°C but the faulty batch was finished by a subcontractor in a relatively chilly Midlands town bordering Wales. No other batches from this source were affected and it seems likely that the faulty batch was the first to have been prepared on a Monday morning before the factory had warmed up.

The defective catheter mounts were not spotted at the final inspection, and the anaesthetist also failed to see the split, despite his routine of expanding the device and closing it before use. The reason is probably that corrugations at the extreme ends of the catheter do not open as easily as those in the middle and the device has to be pulled apart firmly to be sure of opening all the corrugations. Curiously, the Superset model is not pressure tested for leaks like other types of flexible catheter mount made by the same manufacturer.

Conclusions

Faults arising in a proportion of mass-produced disposable products, especially those distributed in thousands throughout the country, are a particular cause for concern, because of the difficulties associated with the task of warning all potential users without delay and ensuring that all stocks are examined. These stocks may be in transit, at wholesalers or scattered throughout institutions where they are not necessarily used in rotation according to their date of delivery. Whilst some items will still be batched in their boxes others may well be on shelves in a kind of 'pick and mix' with samples from different batches. The prime lessons are clear: disposable equipment should only be purchased from well-established manufacturers and suppliers who can guarantee batch-traceability, and all stocks held by hospitals and clinics should be used in a properly regulated manner. Cost-conscious managers should beware of the extra complications introduced into the system when they shop around for bargains between suppliers.

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APPARATUS

Whole blood electrolyte assay using ChemPro 500

A comparison of assay performance with standard laboratory instruments

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Summary

The ChemPro 500 'near-the-patient' analyser, with ChemPro 'Ion Profile' sensor cards, was evalutated for the assay of pH, Ca^{2+}, K^{+} and Na^{+} in whole blood samples from patients in the intensive care unit or during surgery for heart or major blood vessel disease, or for liver transplantation. Imprecisions estimated from replicate whole blood measurements were much greater for all four ions than even the least stringent of the generally accepted analytical goals, and much greater than those estimated using quality assurance materials. Comparisons of assayed values with those obtained using standard laboratory instruments showed significant constant and proportional biases. The performance of the ChemPro 500 with the Ion Profile cards gave us no confidence in recommending their use to anaesthetists and intensivists.

Key words

Measurement techniques; ion-sensitive electrodes.
Ions; hydrogen, calcium, sodium, potassium.

Recent advances in technology have led to the availability of a profusion of devices which carry the generic title of microsensors. These are physically small items of equipment which, using a variety of semiconductor techniques, are able to make a rapid measurement of physical, chemical or biological variables. They are often called biosensors when they are used to measure biological variables (for a recent review see Rolfe[1]). Some biosensors (e.g. those which measure blood glucose) are already in clinical use and there is considerable interest in the development of others.

The importance of this new technology to the anaesthetist and intensivist is that tests may be performed rapidly, in the operating theatre or at the bedside, and immediate therapeutic action may be initiated. The data obtained must be both precise and accurate (see Appendix for definitions of these terms). The fear of poor quality control is real and has been the subject of a recent editorial[2] in which the problems of 'side-room' tests were discussed.

Concern over the accuracy and precision of extra-laboratory tests performed by clinicians is not new. A controversy over the use of automated blood gas estimations raged over a decade.[3] Such machines are now well established, but bedside tests in general are viewed by biochemists as likely to yield poorer quality results.[4] The major worry expressed by clinical biochemists is that whilst the responsibility for the reliability, accuracy, precision and calibration of the equipment rests with them, clinicians working alone will nevertheless produce inaccurate, imprecise results.[5] Despite these fears, interested clinicians have produced very acceptable results using centrifuged blood assayed with standard laboratory equipment kept in an intensive care unit (ICU).[6]

However, several instruments not only transfer the responsibility to the clinician, but also introduce new sensor technology. It is extremely likely that, in a working environment in which costs are becoming increasingly important, anaesthetists and intensivists will sooner or later find themselves being asked to undertake 'near-the-patient testing', so as to reduce the call-out costs of technicians. It is therefore important that such instruments are tested under realistic working conditions with widely varying patient pathologies, so that clinicians can act confidently on the results which they obtain in such circumstances.

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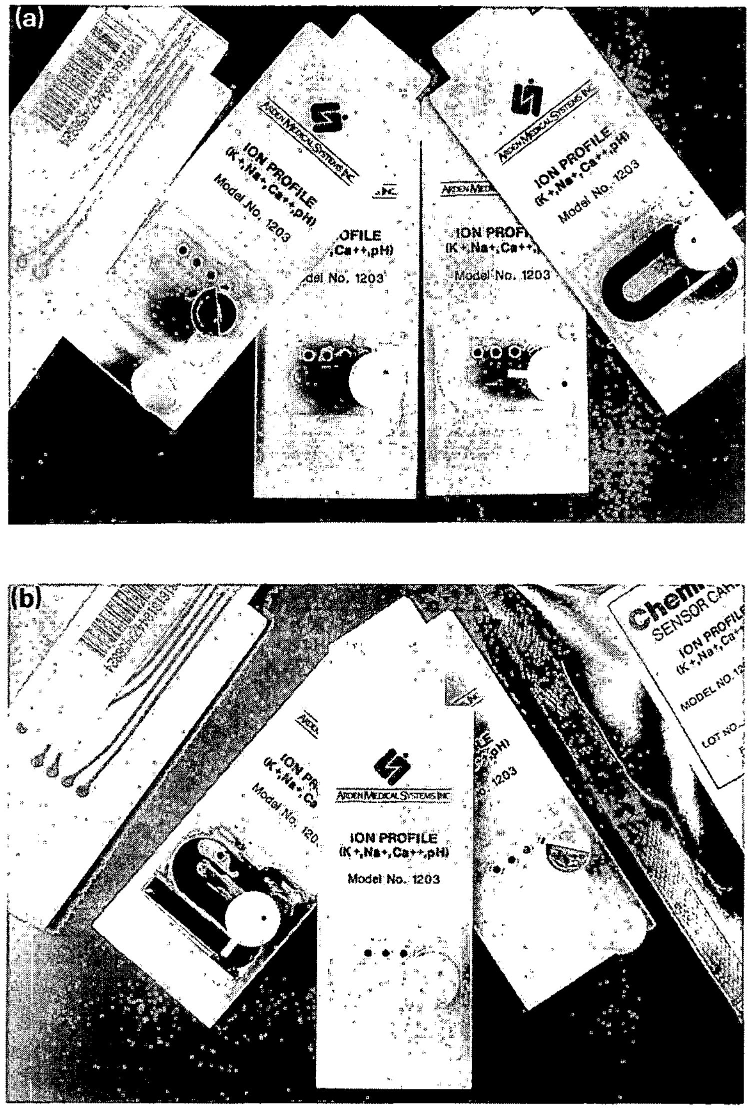

Fig. 1. (a) ChemPro Ion Profile sensor cards for measurement of pH, K^+, Na^+, and Ca^{2+} in whole blood. The photograph shows, from left to right: the underside of a sensor card with the bar code and printed circuit board tracks from electrodes to edge connectors; sensor card with blood in sample pot; sample lid closed; sample pot turned one quarter turn to release calibrant; sample pot turned a further half turn to release blood. **(b)** ChemPro Ion Profile sensor cards. The photograph shows, from left to right: inverted card; card in which flow of calibrant across sensors was faulty (the calibrant was released by a quarter turn of the sample pot and the faulty flow pattern was visualised by release of a red dye solution, instead of blood, by a further half turn of the sample pot); card with sample pot lid in closed position; lid in open position; sealed package containing sensor card.

The ChemPro 500 is a new 'near-the-patient' clinical chemistry system designed for ease of use. It operates with single-use ion-selective (ISE) sensor cards (Fig. 1(a)). It is a modified version of the ChemPro 1000, which has been the subject of a number of recent evaluations.[7–10] However, none of these studies included blood samples representative of both normal biochemistry and the range of pathologies encountered in anaesthesia and intensive care, nor did they indicate the frequent faulty card behaviour encountered in this study and discussed in more detail below. The manufacturers also claimed that the performance of these sensor cards had improved since the other evaluations were published. The ChemPro 500 differs from the ChemPro 1000 in its internal software and in the number of function keys on the operating panel.

The evaluations reported here were concerned particularly with the performance when making measurements on heparinised whole blood samples, because this is likely to be the most frequent mode of use in the ICU and operating theatre environments.

Special attention is drawn to the dangers of assessing clinical chemistry instruments solely with standard quality control sera and then extrapolating such imprecision estimates to measurements made on whole blood samples.

Materials and methods

Instrumentation

The ChemPro 500 (Arden Medical Division, Johnson Diagnostics, Johnson and Johnson Inc, St Paul,

Minnesota, USA) was supplied on loan by the UK distributor* at the time of testing. 'Ion Profile' cards to measure pH, Na^+, K^+ and Ca^{2+} with the ChemPro 500 were purchased from the UK distributor.

The cards perform direct ion-selective measurements using unthermostatted 'coated wire' type ISEs and each card incorporates a reference electrode. On each card is a container, which has a sealed calibrant solution compartment and a compartment into which the blood sample is placed (capacity 0.15 ml). On the underside of the card is a bar code which contains information on the types of sensors on the card, as well as batch quality control information.

The sample of blood is put into the sample compartment, the container is capped, and the sensor card inserted into the ChemPro 500. Appropriate instructions are displayed on the LCD screen, and the operator turns the cap of the sample container to release the calibrant into the sensing compartment (which fills by capillary action). There follows an initialisation period, in which the sensors' operating characteristics are determined. If this initialisation is satisfactory, the operator is instructed to turn the cap of the sample container a further half turn in order to release the blood into the sensing compartment. The results are displayed on the LCD screen, at the end of the measurement period, and are also printed as a permanent record.

During this evaluation, a considerable number of sensor cards failed to initialise because, when the calibrant solution was released, it did not flow over all the ion sensors in the array, as illustrated in the photograph in Figure 1(b). Thirty-six cards were used in the trials with quality assurance materials and an additional 150 cards were used in the whole blood trials. The distributors were asked to supply two additional packs of 25 cards each to allow for the initialisation failure (43 cards out of a total of 250 cards failed).

A Radiometer KNA1 sodium/potassium analyser, a Radiometer ABL300 blood gas analyser and two Radiometer ICA1 ionized calcium analysers (Radiometer UK Ltd, Crawley, W Sussex, UK) were used in this series of comparisons of the ChemPro 500 and the Ion Profile sensor cards. The KNA1 and ABL300 were situated in the side-room laboratory of the ICU. Both ICA1 analysers were situated in the emergency clinical chemistry laboratory of the hospital; blood samples were sent to the laboratory by means of a rapid transit system. One of the ICA1 analysers was situated in the operating theatre anteroom when measurements were being made for liver transplantation surgery.

Comparative measurements

Quality assessment materials. 'NOVA Stat Control (A)' materials (Nova Biomedical) were used. The manufacturer states that these materials were developed for quality assessment of ISE instruments and were designed to mimic the properties of human serum. Twelve replicate measurements of a sample of each level (low, normal and high) of the NOVA materials were made with the Ion Profile cards and the ChemPro 500 and also with the three Radiometer instruments. The means and standard deviations for each set were calculated and from these the coefficients of variation were calculated and used as estimates of imprecision.

Heparinised whole arterial blood samples. Samples were collected from arterial lines into 5 ml syringes minimally heparinised with calcium titrated heparin (2100 IU/ml, Ciba-Corning Diagnostics, Halstead, UK). Samples were collected from patients who were treated in the ICU, and from patients during surgery for heart or major blood vessel disease, or liver transplantation. All samples were collected for routine patient management. Two kinds of measurements were performed on whole blood samples. Firstly, as with the quality assessment materials, a series of replicate measurements was made on a series of patients' samples in order to estimate imprecision. The individual variances for each set of replicate measurements were combined in the standard way[11] to obtain the overall variance. Then this variance was used to calculate the standard deviation for calculation of the coefficient of variation. Secondly, a series of samples was measured on both the ChemPro 500 and the various Radiometer instruments for comparison by means of correlation and regression analysis. Correlation and least squares linear regression analyses were performed using the statistical software package Statgraphics PC.

Results

Table 1 shows the results of the imprecision tests with the NOVA materials and Table 2 shows those obtained with whole blood samples. Table 3 shows the results of the regression analyses for comparisons of the ChemPro 500 with the various Radiometer instruments in assays from heparinised whole arterial blood samples. These show the extent of scatter in the comparisons with the Radiometer instruments, and enable a clearer interpretation of the correlations to be gained.

Discussion

What are the most satisfactory criteria against which the statistical estimates of accuracy and precision for a given assay should be compared, in order to be clinically useful and meaningful? This is not easy to answer. The problem has been addressed by Frazer[12] who reviewed various approaches, including those of Elevitch,[13] Tonks[14] and Barnett.[15] These various imprecision goals are listed in Table 4. Frazer[12] favoured the more stringent approach using intra-individual biological variation as the basis for choosing imprecision criteria.

Comparisons of the results of the imprecision tests using NOVA quality control materials for the ChemPro 500 obtained in this study with the results for the ChemPro 1000 published by Ng *et al.*[7] show agreement for ionised calcium concentrations in the range 1.1–1.3 mmol (level 2 material). However, at all three ionised calcium concentrations, the ChemPro 500 was unsatisfactory and did not comply with any of the criteria listed in Table 4 (with the exception of the result for level 2 compared with the least stringent criterion proposed by Tonks).[14]

The imprecision performance for hydrogen ion measurement using the NOVA materials with the ChemPro 500 was best with the middle range NOVA material (level 2). Outside this middle range, the values of coefficient of variation were much less satisfactory.

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Table 1. Reproducibility of assays (as coefficients of variation) using the ChemPro 500 assessed using NOVA Stat quality assessment materials compared with the Radiometer ABL300, KNA1 and ICA1 (see text for details). Twelve replicate assays were performed on each of the three levels of the NOVA Stat materials.

Hydrogen ion	Coefficient of variation (%)	
Analyte concentration	ChemPro 500	Radiometer ABL300
69.2 nmol	3.7	0.06
38.0 nmol	1.75	0.25
9.8 nmol	8.0	0.63
Sodium ion	Coefficient of variation (%)	
Analyte concentration	ChemPro 500	Radiometer KNA1
126 mmol	4.24	0.91
139 mmol	1.54	0.37
167 mmol	2.62	0
Potassium ion	Coefficient of variation (%)	
Analyte concentration	ChemPro 500	Radiometer KNA1
2.4 mmol	6.1	4.6
3.9 mmol	2.6	1.6
6.6 mmol	4.3	1.1
Calcium ion	Coefficient of variation (%)	
Analyte concentration	ChemPro 500	Radiometer ICA1
1.76 mmol	5.2	0.48
1.27 mmol	3.3	0.42
0.66 mmol	9.7	0.84

The imprecision results for sodium ion measurement with the NOVA materials on the ChemPro 500 are unsatisfactory by any of the criteria in Table 4. Comparisons with the results published by Ng *et al.*[7,9] for the ChemPro 1000 show that much greater imprecision was detected in the present study.

The potassium ion imprecision results for the ChemPro 500 are good for the middle range (NOVA level 2), being close to the most stringent criterion of Elevitch.[13] However, the coefficient of variation is much worse with low and high level NOVA materials. The Radiometer performed well with NOVA levels 2 and 3 but, surprisingly, much less well at low concentrations.

The results are very different with whole blood. The imprecision values (as estimated by the coefficient of variation) for all the ion measurements performed using the ChemPro 500 were much greater than any of those listed in Table 4 and were also higher than those reported in previous evaluations of the ChemPro 1000.[7-10] This may be because of the inclusion in this work of samples for assay from a wider range of pathological ion concentration values, and of other pathological biochemistries likely to be encountered in ICU and in operating theatres, which thereby provided a more severe test of performance.

The regression analyses of the comparisons using whole blood show poor correlation coefficients except for hydro-

Table 2. Reproducibility of whole blood assays using the ChemPro 500 and ChemPro Ion Profile cards and, respectively, the Radiometer ABL300, KNA1 and ICA1.

	Coefficient of variation (%)	
	ChemPro 500	Radiometer ABL300
Hydrogen ion	8.50	0.99
	ChemPro 500	Radiometer KNA1
Potassium ion	10.70	1.58
Sodium ion	4.28	0.67
	ChemPro 500	Radiometer ICA1
Calcium ion	11.10	1.77

Table 3. Comparison of assays in whole heparinised arterial blood by the ChemPro 500 with the Ion Profile cards and the Radiometer ABL300, KNA1 and ICA1 using linear least squares regression analysis.

Hydrogen ion	ChemPro 500 versus Radiometer ABL300
regression coefficient	1.14
intercept (nmol)	−6.1
correlation coefficient	0.94
Sodium ion	ChemPro 500 versus Radiometer KNA1
regression coefficient	0.56
intercept (mmol)	56.0
correlation coefficient	0.59
Potassium ion	ChemPro 500 versus Radiometer KNA1
regression coefficient	0.88
intercept (mmol)	0.26
correlation coefficient	0.81
Calcium ion	ChemPro 500 versus Radiometer ICA1
regression coefficient	0.83
intercept (mmol)	0.10
correlation coefficient	0.63

gen ion assay. Analyses of residuals of these regressions demonstrate wide scatter and several large outliers, which contribute to the low correlation coefficients listed in Table 3. The lack of thermostatting would be expected to affect the measurement of both calcium and hydrogen ions as Metzger and Kenny[8] have already demonstrated with the ChemPro 1000. However, residuals analysis of the regression for hydrogen ion demonstrates relatively small scatter, strongly suggesting that the temperature variation must have been small for the set of measurements performed over a period of weeks for this evaluation. Thus, amongst the major contributors to the scatter in the regressions for calcium, sodium and potassium will be the variations in the responses of the ion-selective membranes to the variability of the matrix (blood composition variations) and the variability in the process of manufacturing of the ion-selective membranes and the reference electrodes on the Ion Profile sensor cards.

The evaluation of the performance of the ChemPro 500 with the Ion Profile cards demonstrates the difficulty of relating performance with quality assessment materials which have ion concentrations near the population mean to those with more pathological values, or to the performance with whole blood. A major area of application of the ChemPro 500 is likely to be the assay of whole blood specimens without repetitive sampling, but the results of our evaluation do not inspire confidence in the measurements obtained. This is especially so at and beyond the extremes of the 'normal' range, when 'near-the-patient' testing is most likely to be of value to the anaesthetist or intensivist.

Table 4. Various analytical goals for imprecision (as coefficient of variation, %).

	Source of recommended analytical goal		
Analyte	Elevitch[13]	Tonks[14]	Barnett[15]
Calcium	0.9	5.4	2.3
Potassium	2.2	5.4	4.2
Sodium	0.4	1.1	1.3

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Appendix
Definitions of accuracy and precision

Accuracy. This is a measure of how close the measured value is to the actual value and represents the bias in a measurement method. In a comparison of methods by regression analysis, the intercept is the 'constant bias' and the deviation of the slope from unity is the 'proportional bias'.

Precision. This is a measure of the reproducibility or repeatability of a measurement. Common representations of this are the standard deviation and the coefficient of variation.

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HISTORICAL NOTES

Harold King

A notable contributor to anaesthesia

T. C. GRAY

Summary

Harold King was an analytical chemist of distinction, who worked with Sir Henry Dale and his colleagues in the Medical Research Institute, later the Medical Research Council. He helped to quash the theory that the anaesthetic action of ether was attributable to its impurities. Interest in alkaloids led to the elucidation of the structure of hyoscine, the synthesis of muscarine and the first isolation of crystalline tubocurarine for which he proposed a structural formula, work which influenced Bovet in the synthesis of gallamine. He proposed the synthesis of the homologous series of methonium compounds which included relaxant and hypotensive drugs. His collaboration with Rosenheim was outstanding and opened the way for synthesis of cholesterol and the steroids. He was always encouraging clinicians, and gave a sample of tubocurarine to Ranyard West who was the first to inject d-tubocurarine into a human patient.

Key words

History; Harold King.

There are important pioneers in the story of anaesthesia whose contributions are not as widely appreciated as they deserve. They are more likely to be scientists than clinicians. Perhaps their names are vaguely familiar, but that is all. One such was Harold King. His contributions to our specialty were considerable.

Early career

King, although of Lancashire stock, was born in Wales and graduated in chemistry with first class honours from University College, Bangor, and was appointed research analytical chemist in the London Gas, Light and Coke Co. After a short time, King moved to the Wellcome Physiological Research Laboratory, where he made his first contact with biological research and with Henry Dale. However, he had to spend the 4 years of World War 1 in the Wellcome Chemical works at Hartford synthesising drugs such as aspirin which could no longer be imported from Germany. After the armistice, King was taken onto the staff of the Medical Research Committee, a statutory body, which was to become the Medical Research Institute and eventually the Medical Research Council. There he was a member of a team led by Dale and he remained working in the Council's laboratories until he took early retirement in 1950. He died 6 years later, aged 69 years.

King's work covered a wide field. In the early 1920s, inspired by the discovery of Salvarsan, he was synthesising prospective chemotherapeutic agents and doing constructive work on arsenicals and antimalarial drugs which later paved the way for the great advances in that field. However, his work impinged on anaesthesia, even at this early stage in his career. A controversy was raging over the anaesthetic effect of ether. Was it due to the ether or to the impurities in it?[1] King with Dale and a young anaesthetist on the staff of St. Bartholomew's Hospital, C.F. Hadfield, in a classical paper concluded that their 'observations give no support to the statements that pure ether is devoid of anaesthetic action, that the activity in this direction of ordinary ether is due to impurities and that the removal of impurities improved the potency of the ether.'[2] Hewer, strangely enough, did not agree and in the same issue of the *Lancet* suggested clinical evidence for his disagreement.

Alkaloids and tubocurarine

From the start King had intense interest in the chemistry of alkaloids. He revealed the complicated stereochemistry of hyoscine[3] and in 1922 isolated muscarine.[4] It was in this field that he made his major contributions to our specialty.

Henry Dale gathered around him a brilliant group of scientists in the Medical Research Institute, Vogt, Brown,

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Fig. 1. Harold King, 1887–1956. (With permission of the Biographical Memoirs of the Royal Society.)

and Feldburg. They were to become stars in the physiological firmament, and were involved in fundamental work on neuromuscular transmission, so it was not surprising that King should turn his attention to curare. It was a useful investigatory tool and a substance with great pharmacological potential, if only the component responsible for its paralysant activity could be identified, purified and administered with accurate posology. King's work on the alkaloids of curare has been described as 'A classical exercise in organic chemistry which led to results of far reaching importance in pharmacology and therapeutics.'[5] In the 13 years, 1935–1948, he published no less than 10 papers on the curare alkaloids. The two most important appeared in 1935. In the first of these, he described the isolation from tube curare of a crystalline alkaloid.[6] The German chemist Boehm had classified curares into Pot, Calabash and Tube according to the container used for the curare by the Indians around the Amazon and Orinoco Rivers[7] and in 1897, he had separated an amorphous alkaloid from tube curare which he named 'tubocurarine'.[8] Similarly, King named the dextro-rotatory crystalline alkaloid which he had isolated from tube curare, 'tubocurarine'. He established its structural molecular formula as a bisbenzyl isoquinoline derivative, so containing two quaternary ammonium groups.[9] This work of 55 years ago has only recently been challenged, to the extent that probably only one of the nitrogens is quaternary.

It is interesting to find that King investigated the alkaloids present in samples of the chondodendron family of plants. However, none of his material yielded tubocurarine and it was left to Wintersteiner and Dutcher,[10] 8 years later, to be the first to extract crystalline tubocurarine from a known plant source. The writer is not aware of any plant source for tubocurarine, other than the *Chondodendron tomentosum*: so, if that is correct, King must have isolated his crystalline alkaloid from the *chondodendron*, although he did not know it.

Bovet, the discoverer of the first synthetic nondepolarising relaxant, gallamine, acknowledged his indebtedness to King.[11]

The onium compounds

William Paton, an Oxford and University College Hospital graduate pharmacologist, later to become an Honorary Fellow of the Faculty of Anaesthetists of the Royal College of Surgeons, was working in the Research Institute after the Second World War. He has related how in 1945/46 he was investigating various compounds for histamine release. One of these, a straight chain compound, had eight methyl groups separated by two quaternary ammonium radicals. When he injected this into a cat, the animal stopped breathing. He was astonished by this response. On investigation, he found that the apnoea was due to a curare-like action. He realised the importance of this observation, but, as the octamethonium had clinically undesirable effects, he consulted King. King suggested that a series of these straight chain compounds, C2 to C12, should be synthesised in the hope of finding one with only a paralysant effect and he asked a young research pharmacological chemist from Greece, Eleanor Zaimis, who was working in the Institute, to do the synthesis. The compound with the two quaternary groups separated by 10 methonium groups, decamethonium, was found to have powerful neuromuscular blocking activity and was otherwise pharmacologically inert. It was introduced into clinical practice by Organe.[12] The compound with five carbon atoms reversed the decamethonium block. However, hypotension due to sympathetic block made it an unsuitable antagonist.

Paton and Zaimis published their discovery in *Nature* on 16 March.[13] The letter immediately preceding theirs was one from Barlow and Ing,[14] working in the Department of Pharmacology at Oxford, who also reported the paralysing action of the straight chain methonium compounds and that the deca- compound was the most active and apparently with no other effects. Ing had for a long time been interested in quaternary ammonium compounds other than the methonium group and had written a review of their neuromuscular blocking activity 10 years previously.[15] Whereas Paton had stumbled upon the relaxant action of these compounds, Ing conceded that he had arrived at it through knowledge of King's work on the formula of tubocurarine. He considered that the straight chain methonium compounds were likely to be less rigid molecules and more adaptable to the varying inter-receptor distances at the muscle endplate than weighty molecules such as tubocurarine and that this accounted for their greater potency. He reminded his readers that the original demonstration of the curareform activity of onium compounds was by Crum Brown and Fraser working in Edinburgh in 1968.[16,17]

In 1951, Scurr described the use of hexamethonium (C6) for the production of controlled hypotension during operation.[18] This was the first clinical attempt to lower blood pressure pharmacologically and hexamethonium was

seen by physicians to open up a new era for their patients suffering from high blood pressure.

Steroids

King will be revered by anaesthetists for making tubocurarine available, but it has been suggested that King will be best remembered, by scientists, for his purely theoretical work done in collaboration with Rosenheim, between 1932 and 1934, on the revamping of the formulae of cholesterol and related steroids.[19–23] It led to the synthesis of vitamin D,[24] the steroids, adrenocortical hormones, sex hormones and also the narcotic and relaxant steroids, such as althesin and pancuronium. There will probably be others to follow. It has been claimed that their theorising 'will stand in the history of organic chemistry as one of those few ideas that have revolutionised a whole branch of the subject.'[5]

The clinicians' friend

King was a shy, quiet and retiring man. He was essentially a backroom worker and appeared happiest when at his bench in the laboratory. He was always ready to listen to others in less strictly scientific disciplines, especially to clinicians, to advise and propose plans for research. Apart from holidays in Ireland, it appears that he only left this country once and that was during the war, when he went to the USA as Secretary of the Committee on the synthesis of penicillin. His work was recognised by his election as a Fellow of the Royal Society in 1933 and in 1959 he was awarded a CBE.

One of the clinicians who contributed to the early curare story and whom King helped and encouraged was Robert George Ranyard West. He was a lecturer first in physiology at St. Bartholomew's Hospital and later in pharmacology at Oxford. West made many attempts to use curare clinically in patients suffering from spasticity and tetanus, but with frustrating results because of the unpredictability of crude curare and of his inability to control respiration and bronchial secretion. He consulted King and begged samples from him of various curares for clinical trial. He thought some offered relief of the muscular spasm without causing paralysis and he called this a 'lissive' effect. It would certainly be very useful clinically if such an effect were possible. Among the samples King gave to West was crystalline tubocurarine and he delivered a paper on its effects to the Royal Society of Medicine in March 1935.[25] He described how he gave subcutaneous doses of from 5–50 mg to a patient with spastic paraplegia and had carefully observed and recorded its effects. He recorded that tubocurarine did not have as good a lissive effect as crude curare. West was, therefore, the first to administer King's d-tubocurarine to a human patient, but lack of expertise in supporting respiration was his main difficulty. He was a man just before his time! It is galling to appreciate that tubocurarine was available to anaesthetists who, certainly since the advent of cyclopropane in the early 1930s, were skilled in controlling pulmonary ventilation. It took the courage of Harold Griffith in 1942 to take the first step to revolutionise anaesthesia and surgery.[26]

West's relationship with King is delicately described by West in the *Journal of Medical History*: 'Reviewing my correspondence with Harold King, I see that 1936 was a very busy year. I chivvying, he patient, if occasionally expostulatory! I had plenty of pharmacology to do on King's many fractions, but no new successes in treating human spasticities to report.' Rather plaintively, he continues: 'I think I overestimated the degree to which those in authority on the Medical Research Council staff shared my enthusiasm.'[27]

Conclusion

Harold King was a distinguished scientist. He contributed 129 papers between 1911 and 1956, many seminal and a good proportion relevant to anaesthesia and general medicine.

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Anaesthesia, 1991, Volume 46, pages 683–686

Forum

Cardiovascular effects of nasotracheal intubation

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Summary

Intubation time, arterial pressure, heart rate and arterial oxygen saturation during nasotracheal intubation effected with the Macintosh laryngoscope blade were compared with those during orotracheal intubation. The 60 patients studied received a standardised general anaesthetic and were randomly allocated to one of two groups immediately before tracheal intubation. The mean nasal intubation time (33.2 seconds) was significantly greater than mean oral intubation time (14.8 seconds). The mean arterial pressure changes in the nasal group were significantly greater and more prolonged than in the oral group. The mean heart rate in the nasal group was significantly lower than in the oral group during the first minute after intubation, after which heart rates were similar. There were no significant differences between the two groups with regard to arterial oxygen saturation levels at any stage.

Key words

Anaesthesia; general.
Intubation; nasotracheal.
Complications.

The pressor response to tracheal intubation has been extensively investigated, as have the various pharmacological methods of attenuating it.[1,2] However, the cardiovascular disturbances produced by nasotracheal intubation have received less attention. This study was therefore designed to assess the heart rate, and arterial pressure changes in a group of patients undergoing nasotracheal intubation using a Macintosh laryngoscope compared to a control group undergoing orotracheal intubation.

Method

The investigation was approved by the ethics committee of the South Birmingham Health Authority and informed written consent was obtained from each patient. Sixty ASA class 1 patients aged between 16 and 55 years undergoing elective surgery requiring tracheal intubation and mechanical ventilation of the lungs were studied. Twenty five participants were scheduled for ear, nose and throat (ENT) surgery, mainly tonsillectomy, and the remainder were gynaecological or general surgery patients. Patients taking vasoactive drugs, those who were morbidly obese, or who had a history of nasal obstruction or expected to be difficult to intubate were excluded from the trial.

Patients were premedicated one hour before surgery with oral temazepam 20 mg. An indwelling intravenous cannula was sited and continuous ECG monitoring was established in the anaesthetic room. Heart rate and arterial oxygen saturation were monitored continuously and arterial pressure at one minute intervals by means of a Dinamap 1846SX monitor and recorded by a Dinamap TR2000 printer. After a stabilisation period of at least 5 minutes, baseline recordings were made and anaesthesia was induced with thiopentone 5 mg/kg, followed by atracurium 0.5 mg/kg. The patient's lungs were ventilated with oxygen 50%, nitrous oxide 50% and isoflurane 1% by means of a Guedel airway and facemask attached to a Bain system with an initial fresh gas flow of 90 ml/kg/minute. Carbon dioxide concentration was monitored with a Nellcor N-1000 capnograph and fresh gas flow and ventilation were adjusted to maintain the end-expired carbon dioxide concentration at 4.5–5%. After 4 minutes' ventilation, patients were assigned, on a random number basis (stratified by sex, using sealed envelopes) to either the oral or nasal intubation groups and the Dinamap arterial pressure monitor was switched to standby mode while the appropriate procedure was performed. All intubations were carried out using direct laryngoscopy with a Macintosh laryngoscope, and Magill's forceps were used if necessary. For nasal intubations, the right nostril was selected, but if resistance was encountered, the left nostril was used. Disposable, cuffed, Portex tracheal tubes, lubricated with KY jelly, cathetermount attached (size 8 mm for males and size 7 mm for females) were used in all cases. As soon as successful tracheal intubation was verified, an arterial pressure determination was initiated and five further recordings were obtained at one-minute intervals. The intubation time was taken as the interval between removal of the facemask from the patient's face and reconnexion of the Bain system to the catheter mount after the intubation had been completed. If any intubation could not be completed within 60 seconds, the patient was withdrawn from the trial and his/her assignment card was resealed in an envelope and randomly placed among the remaining envelopes to be used later.

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Table 1. Age, weight and sex characteristics. Data expressed as mean (SEM) where applicable.

	Age (years)	Weight (kg)	Sex
Oral group (n = 30)	33.9(1.8)	64.0(2.0)	6M 24F
Nasal group (n = 30)	30.0(1.9)	65.5(2.3)	6M 24F

Table 2. Time to achieve successful intubation.

Group	Number	Mean (SEM) time; seconds	Range; seconds
Oral	30	14.8(1.1)	8–34
Nasal	30	33.2(1.8)*	20–53

*p < 0.05 compared to oral group.

Pulse oximetry data were analysed by the Mann–Whitney U test. Other data were analysed using Student's t-test (paired within groups and unpaired between groups). A p value of less than 0.05 was taken as significant.

Results

The two groups were similar in respect of age, weight and sex distribution (Table 1).

The intubation of two patients in the nasal group could not be completed within the 60 seconds allocated and these patients were withdrawn from the trial. Details of the other intubation times are shown in Table 2. The mean time to complete nasal intubation was 33.2 seconds which was significantly greater than that required to complete oral intubations (14.8 seconds).

Systolic arterial pressures before induction and before intubation were similar in each group (Table 3 and Fig. 1). Induction of anaesthesia caused a significant decrease in systolic pressure in each group, while tracheal intubation caused a significant increase in systolic pressure compared to values before induction in each group. Systolic pressure remained significantly elevated for 2 minutes in the oral intubation group and for 4 minutes in the nasal group. The systolic pressure in the nasal group was significantly greater than that in the oral group during all five postintubation minutes and diastolic pressures followed a similar pattern except that the diastolic pressure in the nasal group was significantly greater than that in the oral group during the third and fourth minutes after intubation (Table 3 and Fig. 1).

Mean heart rates before induction and before intubation were similar in each group (Table 4 and Fig. 2), and there were significant increases in mean heart rate after induction of anaesthesia in each group. Tracheal intubation caused further significant increases in heart rate compared with values before intubation in each group, and compared to pre-intubation values were sustained for 3 minutes in each group. The mean heart rate in the nasal group was significantly lower than that in the oral group during the first minute after intubation, after which they were similar.

Discussion

Many aspects of the cardiovascular effects of nasal intubation have been investigated previously. In 1971, Pryce-Roberts *et al.*[2] detected no arterial pressure or heart rate changes when four blind nasal intubations were carried out with the aid of carbon dioxide-induced hyperpnoea under general anaesthesia. However, Hartigan *et al.*[3] observed a significant pressor response associated with blind nasal intubation under fentanyl, thiopentone and suxamethonium anaesthesia and studied the efficacy of lignocaine, either injected intravenously or applied topically, in attenuating it. Ovassapian and colleagues[4]

Table 3. Mean (SEM) values of arterial blood pressure (systolic and diastolic, mmHg) in oral intubation and nasal intubation groups.

Group	Before induction	Before intubation	Time after intubation; minutes 1	2	3	4	5
Oral (n = 30)							
Systolic	126(3)	115(3)−	145(4)+	135(3)+	124(3)	118(3)−	113(3)−
Diastolic	71(2)	67(2)−	89(2)+	78(2)+	70(2)	66(2)−	62(2)−
Nasal (n = 30)							
Systolic	124(2)	119(2)−	158(5)+*	147(4)+*	136(3)+*	130(3)+*	125(3)*
Diastolic	69(2)	66(1)−	92(3)+	81(2)+	75(2)+*	70(2)*	65(2)−

+ −p < 0.05 compared to pre-induction values; *p < 0.05 compared to oral intubation values.

Table 4. Mean (SEM) values of heart rate (beats/minute) in oral intubation and nasal intubation groups.

Group	Before induction	Before intubation	Time after intubation, minutes 1	2	3	4	5
Oral (n = 30)	80(2)	91(2)	107(3)+	102(2)+	97(2)+	92(2)	88(2)
Nasal (n = 30)	78(3)	90(2)	99(3)+*	99(3)+	95(3)+	90(3)	85(2)−

+ −p < 0.05 compared to pre-intubation values; *p < 0.05 compared to oral intubation values.

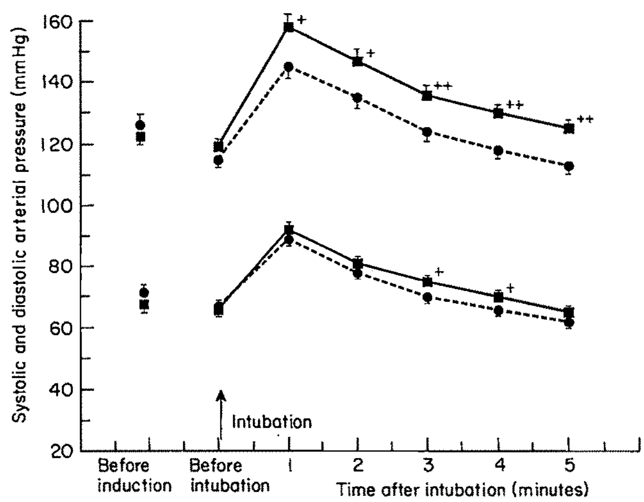

Fig. 1. Systolic and diastolic arterial pressures (mean, SEM) in the oral and nasal intubation groups before induction of anaesthesia and for 5 minutes after intubation. – – – –, oral intubation group; ———, nasal intubation group. $+p < 0.05$, $++p < 0.005$ between groups.

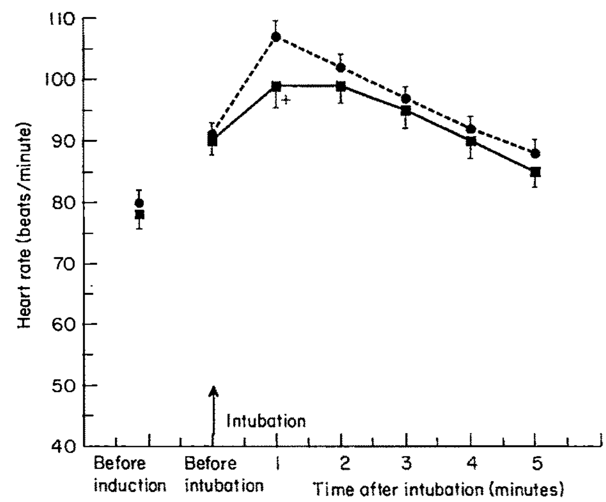

Fig. 2. Heart rates (mean, SEM) in the oral and nasal groups before induction of anaesthesia and for 5 minutes after intubation. – – – –, oral intubation group; ———, nasal intubation group. $+p < 0.05$ between groups.

reported that the haemodynamic changes were minimal when fibrescope-guided nasal intubation was performed on awake but sedated patients under local anaesthesia. Fletcher *et al.*[5] found no differences in heart rate, arterial pressure or sedation requirements during mechanical ventilation of the lungs using either an oral or a nasal tracheal tube following cardiac surgery. The cardiovascular effects of nasotracheal intubation following direct laryngoscopy with the Macintosh laryngoscope under general anaesthesia were compared with those following blind nasal intubation by Meiklejohn and Coley[6] and with those following fibrescope-guided nasal intubation by Smith and co-workers.[7] However, the cardiovascular changes of nasal intubation have not been compared with those of oral intubation.

This study has shown that the hypertensive response to nasal intubation of the trachea under general anaesthesia is significantly greater and more sustained than that of oral intubation. However, the tachycardia associated with nasal intubation is significantly less than that of oral intubation during the first minute after intubation. It seems likely that nasal intubation produces greater mechanical stimulation of the upper airway and that this generates a more vigorous activation of the sympathetic nervous system. Increased intubation time may also contribute to the more severe pressor response, since Stoelting[8] demonstrated that increasing the duration of Macintosh laryngoscopy caused a progressive increase in mean arterial pressure. The slower heart rate during the first minute after intubation in the nasal group is less readily explained, but it may be mediated by baroreceptor reflexes in response to a more rapid increase in arterial pressure during nasal intubation. Alternatively, it may be the result of the influence of the nasocardiac reflex. This trigeminovagal reflex arc is analogous to the more widely recognised oculocardiac reflex, and has recently been implicated in the development of profound bradycardia following intranasal instrumentation.[9,10] Sensory nerve fibres supplying the nasal mucosa are carried via the ophthalmic and maxillary branches of the trigeminal nerve to the Gasserian ganglion, thence to the sensory nucleus of the trigeminal nerve in the floor of the fourth ventricle. The efferent pathway is via the vagus nerve to the sinu-atrial node. The sympathetic responses following nasal intubation may thus be counterbalanced by relatively more vagal activity than those following oral intubation, which would account for the observed heart rate differences.

The exaggerated hypertensive response to nasotracheal intubation, while probably of little consequence in young, fit individuals, may represent a serious hazard to patients suffering from cardiovascular disease or to ITU patients subject to cardiovascular instability. The indications for nasal tubes in such patients should be carefully reviewed in the light of the findings of this study. If nasal intubation is still considered advantageous, then effective measures should be implemented to minimise the pressor response.

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A prospective study of liver function in infants and children exposed to daily isoflurane for several weeks

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Summary

Eleven infants and children presenting for daily radiotherapy for a period of at least 2 weeks were anaesthetised with isoflurane in 33% oxygen and nitrous oxide. They were unpremedicated and given no other agents to supplement anaesthesia. The average number of exposures was 24 (SD 11; range 10–39) and the total anaesthetic time per exposure varied between 15 and 30 minutes. Liver function was assessed by determining serum total bilirubin, aspartate amino transferase, gamma glutamyl transferase and alkaline phosphatase before the start of treatment and at 5-daily intervals thereafter. There was no measurable change in any of these determinants of liver function. All children accepted daily induction of anaesthesia with isoflurane. Induction, maintenance and recovery from anaesthesia were uncomplicated.

Key words

Anaesthesia; paediatric.
Anaesthetics, volatile; isoflurane.
Complications; hepatotoxicity
Liver; function, hepatotoxicity.

Infants and young children with malignancy presenting for radiotherapy require heavy sedation or anaesthesia in order that they remain immobile during exposure to radiation (up to 30 minutes). Treatment is often on a daily basis and may extend for a period of several weeks. We have found that general anaesthesia is preferable to heavy sedation because recovery is more rapid and interferes least with the overall well-being of the patient; they can grow and develop as normally as their underlying disease process will allow. It is now recognised that halothane hepatitis occurs in infants and children, and that this is more likely after repeated exposure,[1] although some studies conclude that the incidence is extremely low (1 : 80 000–1 : 200 000).[2,3] Some centres use halothane, even in circumstances where daily exposure on several occasions is called for.[4,5] If the incidence of halothane hepatitis after repeated exposure in children is of this order of magnitude, and if halothane has clearly superior properties to alternative agents in these circumstances, its continued use is at least (arguably) justifiable. In unpremedicated paediatric outpatients halothane has been reported to be superior to isoflurane for induction of anaesthesia because airway irritability, manifest as coughing or breath-holding, is less common.[6] Experienced paediatric anaesthetists appear to have fewer problems with isoflurane[7] and it has been the impression of the two senior authors (J.G.D., R.M.J.) that although halothane provides good conditions for induction of anaesthesia in children, with experience isoflurane could be at least comparable. In a prospective study we investigated liver function in infants and children undergoing daily radiotherapy for malignant disease and determined the overall acceptability of isoflurane for induction and maintenance of anaesthesia.

Patients and methods

After ethics approval and parental informed consent, all infants and children scheduled to undergo daily radiotherapy for a period of 2 weeks or more were studied over the 4-year period 1985–1989. Each treatment took place at about 0830 h on weekdays and patients were always unpremedicated. Anaesthesia was induced with the child sitting on its mother's lap, commencing with 3–5% inspired isoflurane in 66% nitrous oxide and oxygen delivered from a Mapleson E breathing system. Following induction of anaesthesia, monitoring was established using an ECG, pulse oximeter and, when necessary, a respiration monitor incorporating an in-line thermistor. The inspired isoflurane

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Table 1. Demographic data.

Patient	Sex	Age (months)	Treatments	Diagnosis
1	m	18	21	Astrocytoma
2	f	27	10	ALL
3	f	44	25	Astrocytoma
4	f	50	23	Neuroblastoma
5	f	15	27	Optic glioma
6	m	59	35	Neuroblastoma
7	f	58	22	Astrocytoma
8	f	62	30	Optic glioma
9	f	42	39	Medulloblastoma
10	m	25	10	ALL
11	f	23	32	Medulloblastoma

Age refers to age at entry into the trial.
ALL, acute lymphoblastic leukemia.

concentration was then reduced to 2%, and delivered via a facemask strapped to the patient's face. During radiotherapy the children and monitors were observed by closed-circuit television.

Blood was taken for measurement of liver function tests before treatment on the first day and at 5-daily intervals thereafter. The following tests of liver function were performed: total bilirubin, aspartate amino transferase (AST), gamma glutamyl transferase (GT) and alkaline phosphatase (AP).

Results

All results are reported as mean (SD) as appropriate. Eleven children aged 38 (17) months underwent an average of 24 (11) treatments each. The individual patients, their age, number of treatments and diagnoses are shown in Table 1. The total anaesthetic time varied between 15 and 30 minutes and in all patients induction of anaesthesia was without complications, respiratory or otherwise, and no variation in anaesthetic technique was ever necessary. The onset of regular respiration usually occurred in less than 60 seconds of the start of induction of anaesthesia. Maintenance and recovery from anaesthesia were also uncomplicated and all children were able to eat and drink normally within an hour of treatment (within the limitations placed on this by the disease itself).

There was no alteration in liver function throughout the period of treatment (Table 2) although two of the children with acute lymphoblastic leukemia had alkaline phosphatase levels in the high normal range (900–1000 IU/litre).

Discussion

Brett and her colleagues have discussed the anaesthetic requirements of infants and children presenting for repeated radiotherapy.[8] Like us they conclude that appropriately administered general anaesthesia is preferable to sedation (using drugs such as benzodiazepines or ketamine); it allows for more rapid and clear-headed recovery, but needs close monitoring of respiration and oxygenation. These authors used an insufflation technique, but we found that a simple mask was an acceptable alternative; it avoids the need for tracheal intubation and thus the necessity to use deeper levels of anaesthesia or a muscle relaxant. Appropriate monitoring with pulse oximetry, a respiration monitor and an ECG, together with close observation by closed-circuit television, allowed us to be sure of the safety of the patient during maintenance of anaesthesia.

There have been conflicting reports concerning the incidence of respiratory disturbance with isoflurane used for induction of anaesthesia. A number of studies indicate that, compared with halothane, isoflurane induction is accompanied by an increased incidence of cough and breath-holding.[6,9–11] However, like others[7] we have found isoflurane to be entirely acceptable and believe that the continued acceptance of its daily use in our unpremedicated children indicates that, in experienced hands the agent can allow rapid and smooth induction of anaesthesia.

We have also demonstrated, in our small number of patients, that repeated daily exposure to isoflurane does not cause a measurable change in liver function. Even though we were only able to study 11 patients between 1985 and 1989, one 42-month-old girl was exposed to isoflurane 39 times and the total number of exposures in this study was 274. In addition, we were not studying a healthy population and in these circumstances we believe that it was important to use the least toxic agent available. The low solubility and molecular stability of isoflurane suggests that its potential to cause hepatotoxicity should be low. There now seems little doubt that although isoflurane can cause liver injury, the incidence is very much lower than that following halothane.[12]

Kenna and his colleagues have reviewed the topic of halothane hepatitis in children.[1] They have reported the occurrence of this syndrome in seven children aged between 11 months and 15 years and in all cases other causes of liver disease had been excluded; in all but one the diagnosis was confirmed serologically by antibodies to halothane-altered liver cell membrane antigens. All had received more than one documented halothane exposure. The authors review the incidence of halothane hepatitis in children reported in other retrospective studies[2,3] and discuss the inherent problems of this type of study and conclude; 'If only a few cases were missed in retrospective studies this would be sufficient to raise the incidence in children to that observed in adults.'

We have demonstrated that isoflurane is an entirely acceptable agent for the induction and maintenance of anaesthesia in unpremedicated infants and children. In addition, in our study of 11 patients exposed to 274 isoflurane anaesthetics, we were unable to determine any alteration of liver function. In these circumstances we

Table 2. Liver function tests. Mean (SD).

	Control	Day 5	Day 10	Day 15	Day 20	Day 25*
Bilirubin (< 23 μmol/litre)	5.6 (3.8)	4.6 (1.9)	5.8 (2.1)	4.7 (1.4)	5.9 (2.8)	4.7 (1.7)
AST (< 43 IU/litre)	25 (5)	27 (9)	27 (7)	25 (10)	24 (6)	22 (11)
Gamma GT (m 11–54 IU/litre) (f 8–35 IU/litre)	22 (25)	22 (22)	25 (29)	20 (18)	26 (28)	38 (35)
AP (< 1200 IU/litre)**	388 (173)	373 (137)	364 (111)	333 (156)	300 (134)	280 (141)

The values in parentheses indicate the units and the normal range for our laboratory. AST = aspartate transaminase; GT = glutamyl transferase; AP = alkaline phosphatase. *Note that two patients had only 10 days' treatment and four had 20–25 days' treatment. **The normal value in children is up to four times that of adults, which is < 300 IU/litre.

would suggest that in view of the uncertainty concerning the incidence of halothane hepatitis following repeated anaesthesia in children it is difficult to envisage circumstances in which halothane is clearly a superior agent.

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Papaveretum infusions in infants under 6 months of age

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Summary

The effectiveness of a continuous low dose papaveretum infusion for the relief of postoperative pain was assessed in 29 infants aged 1–6 months nursed on the infant surgical ward following major abdominal surgery. Trained nursing staff were able to adjust the dosage within prescribed guidelines and satisfactory analgesia was obtained with a regimen which delivered up to 0.0375 mg/kg/hour, approximately half the dose recommended in children older than 12 months. There was one case of clinically significant respiratory depression.

Key words

Pain; postoperative.
Anaesthesia; paediatric.
Analgesics; papaveretum.

Continuous opioid infusions are known to produce superior postoperative analgesia in children compared to intermittent intramuscular injections.[1] The risks of respiratory depression from fluctuating plasma concentrations with bolus doses are reduced and the pain inherent in the latter technique is avoided. However, the use of opioid infusions in unintubated infants less than 6 months old is contentious. It is usually recommended that such infants be treated as neonates in terms of their sensitivity to the respiratory depressant effects of opioids[2] and infusions avoided in those nursed outside an intensive care setting.

It has been our clinical experience that healthy infants undergoing major (noncardiac) surgery tolerate opioid infusions extremely well on the postoperative ward provided dosage is appropriate and certain guidelines are observed. The aims of this investigation were to evaluate the effectiveness of a low-dose continuous papaveretum infusion, to establish typical dose requirements in healthy infants undergoing major elective abdominal surgery and to document complications.

Methods

Infants aged between 4 and 26 weeks who were to undergo major abdominal surgery under general anaesthesia, and in

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whom extubation and return to the postoperative ward was planned, were considered eligible for the study.

Premedication was with chloral hydrate, 50 mg/kg, administered orally 45 minutes pre-operatively. Intravenous access was established and anaesthesia was induced with thiopentone 4–5 mg/kg and the trachea intubated following administration of a nondepolarising muscle relaxant (alcuronium 0.3 mg/kg or vecuronium 0.1 mg/kg). Anaesthesia was maintained with 33% nitrous oxide in oxygen supplemented with a low concentration of volatile agent (isoflurane or enflurane). The lungs were ventilated mechanically and the end-tidal carbon dioxide concentration monitored.

A standard solution having a concentration of 0.25 mg/ml was prepared by diluting papaveretum 10 mg to 40 ml with 5% dextrose.

A bolus of papaveretum (0.05 mg/kg) was given immediately after induction, followed by a constant infusion of 0.1 ml/kg/hour (0.025 mg/kg/hour). The infusion continued, without alteration, throughout surgery and the recovery period. No other opioids were given. Infusions were administered using a syringe pump (Vickers Treonic or Graseby MS2000), connected to the intravenous cannula by a narrow bore rigid tubing and a Y-connecter containing a one-way valve. Postoperative maintenance fluids were delivered simultaneously through the same cannula using a volumetric pump (Imed).

Postoperatively all patients returned to the infant surgical ward which had well staffed high dependency areas but no facilities for ventilation or invasive monitoring. A trained, experienced nurse made an hourly summary of the infant's sleep and pain state. This assessment was based on observations of distress, restlessness and the quality of cry, and assumed an experienced children's nurse's ability to distinguish crying associated with pain from that due to hunger or other causes.[3]

Infants returned from the operating theatre with the papaveretum infusion rate set at 0.1 ml/kg/hour. Nursing staff were allowed to adjust the rate of infusion within the prescribed range of 0–0.15 ml/kg/hour (0–0.0375 mg/kg/hour) according to their assessment of the infant. All alterations to the infusion rate were documented and staff were instructed to state the reason for any intervention. They were encouraged to decrease the infusion rate gradually after 24 hours where possible.

Routine monitoring included continuous pulse oximetry, and hourly recordings of respiratory rate and skin temperature. All infants were nursed in air on apnoea-sensing mattresses and some infants had nasopharyngeal sampling of end-tidal carbon dioxide concentration.

Statistical analysis was undertaken using the Wilcoxon–Mann–Whitney test.[4]

Results

A total of 1002 infusion-hours were evaluated in 29 patients, 15 of whom were less than 12 weeks old. Patient details are presented in Table 1. There were no neonates in the study although there were two expremature infants, both born at 34 weeks' gestation. One (postconceptual age 49 weeks) had an uncomplicated neonatal period. The other, (postconceptual age 43 weeks), had required ventilation and repair of a tracheo-oesophageal fistula.

Analgesia. The mean postoperative infusion time was 34.8 hours with a range of 6–60 hours. Infusions ran for over 20 hours in all but one infant. Twelve infants were judged completely pain free throughout and three of these required no alteration of the initial infusion rate. Sixteen others had a total of 43 recorded episodes of pain between them, which were easily managed by adjustment of the infusion rate. No infant was assessed as being in pain on more than two successive occasions.

Table 1. Patient details and operative procedures.

Number	29 (20 male, 9 female)	
Ages range	4–22 weeks	
mean (SD)	12 (5.1)	
Weight range	2.9–7.1 kg	
mean (SD)	5.16 (1.2)	
Procedures		
Pyeloplasty		13
Ureteric surgery		7
Laparotomy		5
Ladds procedure		1
Nephrectomy		1
Nissen fundoplasty		1
Diaphragmatic hernia (late presentation)		1

In eight patients the initial infusion rate was increased within the first 6 hours in response to pain, whilst in seven others it was decreased. Seventeen patients required an increase in infusion rate at some time during the first 24 hours. The reasons given for rate increases were pain in 11 infants, restlessness (interpreted as pain) in six and a complex dressing change in one patient. Infusion rates were decreased in response to excessive sleepiness and were decreased in all patients after the first 24 hours. Infants who were judged pain free throughout spent more time asleep than those who were not (87.5% vs 70.4% of the infusion time).

Papaveretum dose. In the first 24 hours postoperatively the mean (SD) dose of papaveretum administered was 0.56 (0.15) mg/kg, with a range of 0.34 to 0.91 mg/kg. The amount delivered per hour ranged from 0.014 to 0.038 mg/kg/hour with a mean of 0.023 (0.006) mg/kg/hour. When analysed separately (Table 2), infants under 12 weeks received slightly less papaveretum than the older infants (mean 0.54 (0.15) mg/kg/24 hours compared to 0.59 (0.15) mg/kg/24 hours) but this difference was not statistically significant. Analgesic requirements did not vary with the nature of the operation.

Complications. When infants were calm or asleep and pulse oximeter readings reliable, oxygen saturations ranged between 94 and 99%. The infusion given to one expremature infant was discontinued at 6 hours following a decrease in respiratory rate, associated with marked desaturation. This incident occurred 2 hours after the infusion rate had been increased and after a total dose of papaveretum of 0.14 mg/kg (0.023 mg/kg/hour) had been administered. A single dose of naloxone was given.

Table 2. Papaveretum requirements in infants greater and less than 12 weeks of age.

	Infants > 12 weeks n = 14		Infants < 12 weeks n = 15	
	Mean	(SD)	Mean	(SD)
Age; weeks	16.5	(3.2)	7.7	(1.8)
Weight; kg	5.9	(0.8)	4.4	(1.1)
Duration of infusion; hours	35.0	(12.9)	34.5	(11.4)
Total dose in first 24 hours; mg/kg/24 hours	0.59	(0.15)	0.54	(0.15)
Infusion rate in first 24 hours; mg/kg/hour	0.025	(0.006)	0.023	(0.006)

One intravenous cannula had to be resited, which led to an interruption of the infusion for one hour and resulted in pain. Nasal itching was common and in one infant was distressing enough for the infusion to be discontinued at 22 hours.

Discussion

Analgesia. The assessment of postoperative pain in infants is based on interpreting behavioural responses and crying. A pain-free infant appears content, sleeps peacefully and is easily comforted while the infant in pain cries distinctively, sleeps fitfully (if at all) and may have a sad expression.[5] However, behavioural responses to pain are also influenced by nonpharmacological factors such as feeding, the presence of a parent and degree of maturity; this makes formal quantification difficult. Spectrographic studies have confirmed that cries of stress, pain and hunger are distinguishable from each other and that a baby's cry can be interpreted correctly by an observer whose skill improves with training and experience.[3] Furthermore 'pain-induced vocalisation' is the only pain-induced behaviour in animals that is blocked by opioids in the range of doses used in humans with clinical pain.[6]

The aim was for a content infant, easily rousable with a normal pattern of sleep. The overall quality of analgesia was good with over 40% of patients assessed as having no pain at all and the remainder easily made comfortable. Infants were not excessively sleepy despite good pain relief.

Dosage. One milligram of papaveretum is approximately equivalent to 0.68 mg morphine. In equipotent doses there is little difference in their analgesic properties although our clinical impression is that children appear more sedated with papaveretum. It has been suggested that the incidence of respiratory depression in neonates is higher with papaveretum than with morphine but this may have been attributable to inappropriately high doses.[7] The manufacturer's data sheet recommends maximum single doses of papaveretum of 0.15 to 0.2 mg/kg in infants below 12 months but avoids suggesting a time interval between doses.[8] There are no published guidelines for papaveretum by infusion. This regimen was calculated to provide 0.15 mg/kg over 6 hours initially, with a maximum dose limit of 0.225 mg/kg (a range approximately half that recommended for children over 12 months). In practice the average requirement was slightly less than the lower of these values.

Previous studies suggest that morphine metabolism approaches the adult pattern in early infancy[9] and that predictable plasma concentrations can be achieved basing infusion rates on body weight.[10] However, as in adults, there may be a considerable interpatient variation in the plasma levels required to produce effective analgesia. This problem remains unaddressed in infants because of the difficulties in measuring pain, but it would suggest that some flexibility in dosing regimens is desirable.

Technique. Safeguards were necessary to ensure the prescribed dose of papaveretum was delivered accurately and to avoid accidental overdosage. The prepared solution was dilute and the syringe contained sufficient volume to avoid the need for frequent refilling. Handling of the syringe, which can lead to inadvertent bolus administration, was therefore reduced to once per 24 hours when a fresh solution was prepared.

A separate intravenous cannula for the papaveretum infusion was not used because venous access is often difficult in this age group. However, should the cannula become blocked, backtracking of opioid solution through the maintenance line could lead to an overdose when the blockage is cleared. We would therefore recommend the use of both a one-way valve connected to the cannula and an infusion pump for maintenance fluids which alarms and stops infusing if backpressure is encountered. As an additional check the residual volume in the syringe was recorded every hour.

Complications. There was one case of clinically significant respiratory depression. It could be argued that opioids should be avoided in all unintubated expremature infants, although this infant had appeared robust and had not required respiratory support during the neonatal period. The other expremature infant in the study was smaller, younger and had already undergone major surgery. She had no problems with the infusion, indeed she required more than the average amount of papaveretum and went on a few weeks after her pyeloplasty to have correction of total anomalous pulmonary venous drainage. These examples illustrate that the term 'expremature' covers a wide spectrum of maturity and physical status and even with conservative dosing some infants will be unpredictably sensitive. As it is probably the sleeping undisturbed infant who is most at risk of respiratory depression, supplementation of intermittent observations with continuous monitoring is essential.

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Pain on intradermal injection with lignocaine

The effect of concentration

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Summary

Twenty ASA 1 volunteers were each injected intradermally with four solutions containing 0.2 ml of 0.5%, 1%, and 2% lignocaine and 0.9% saline to determine whether the pain experienced on injection was related to the concentration of local anaesthetic. A 10 cm linear analogue pain scoring system was used, and the solutions were ranked from most painful to least painful. There were no differences between the different concentrations of lignocaine and 0.9% saline in the severity of pain experienced. We conclude that any concentration of lignocaine may be used intradermally before inserting intravenous catheters without affecting the degree of pain experienced by that injection.

Key words

Anaesthetics, local; lignocaine.
Complications; pain.

Infiltration of the skin with local anaesthetic solution is commonly performed before insertion of an intravascular cannula. It is our usual practice to inject lignocaine intradermally for this purpose. However, the injection of lignocaine itself is often associated with pain,[1,2] and it has been our clinical impression, in common with that of several of our colleagues, that higher concentrations of lignocaine are associated with more pain. Lignocaine, of the commonly used local anaesthetics, has been shown to cause the least pain when injected.[3] It has been demonstrated that lignocaine with adrenaline is more painful than plain lignocaine, and that the addition of sodium bicarbonate to either solution reduces the pain experienced.[4] However, the relationship between concentration of lignocaine and pain has not been determined. We undertook this double-blind, randomised study to investigate that relationship.

Methods

We studied 20 young ASA 1 volunteers, with approval of our local ethics committee, and after obtaining informed consent. Four unidentified solutions containing lignocaine 0.5%, 1%, 2%, and 0.9% saline, were prepared for each subject by our pharmacy and randomly labelled A to D. The volar aspect of the subject's left forearm was marked with four equally spaced circles (labelled A to D in ascending order) from the wrist up to the antecubital fossa. The skin was cleaned with an alcohol wipe, allowed to dry, and 0.2 ml of the corresponding solution was injected intradermally, each from a separate syringe via a 25-G needle in the order A, B, C, D. The injections were made at approximately 30-second intervals, and after each injection the subject was asked to assess the degree of pain on a 10-cm linear analogue scale.[5,6] The solutions were ranked from most painful to least painful based on the frequency with which subjects assigned highest to lowest pain scores. Statistical analysis was by the Kruskal–Wallis test.

Results

There were no significant differences in pain scores between the concentrations of lignocaine or 0.9% saline (Table 1).

Discussion

Skin infiltration with local anaesthetics should ideally be painless, so that the patient experiences minimal discomfort. Morris *et al.*[3] investigated five commonly used local anaesthetic solutions and showed that lignocaine was the least painful. They were unable to relate the degree of pain

Table 1. Median pain scores achieved following intradermal injection of three different concentrations of lignocaine and 0.9% saline.

	0.5% lignocaine $n = 10$	1% lignocaine $n = 10$	2% lignocaine $n = 10$	Saline $n = 10$
Median, interquartile range	0.7 (0.5–1.5)	1.45 (0.7–2.9)	1.3 (0.8–3.1)	0.75 (0.4–2.1)
Range	0–7.1	0–7.4	0–8.5	0–6.3

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to any physicochemical property of the solutions (e.g. pH, sodium chloride concentration, osmolarity or presence of additives), although it has been demonstrated in a different study[4] that adding sodium bicarbonate to lignocaine reduces pain on injection. These authors speculated that the reduction in pain might be due to an increase in the nonionised form of lignocaine.

Our results have indicated that injection of 0.9% saline causes no more pain than any concentration of lignocaine. This is in contrast to two other studies which have shown that 0.9% saline causes either less[4] or more[1] pain than lignocaine. We cannot account for these discrepancies.

Intradermal lignocaine is commonly used to provide anaesthesia for minor surgical operations in addition to aiding pain free insertion of intravenous cannulae. During skin infiltration it is important to minimise any pain caused by the local anaesthetic itself. We have demonstrated that the concentration of lignocaine has no effect on the degree of pain caused by skin infiltration. For cases in which the total dose of lignocaine is not likely to be exceeded, the use of lignocaine 2% may result in a more rapid and intense block, without increasing the pain experienced.

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Anaesthesia, 1991, Volume 46, pages 693–706

Correspondence

Awareness during Caesarean section

As an 'expert' who frequently (all too frequently) is asked to give an opinion regarding awareness during Caesarean section, I was particularly interested in the paper by Lyons and Macdonald (*Anaesthesia* 1991; **46:** 62–4). It illustrates yet again the blindingly obvious, i.e. that awareness is due to too little anaesthetic and is the fault (*not* the bad luck) of the anaesthetist.

The use of minimal anaesthesia in Caesarean section dates from the introduction of relaxants and was said to prevent neonatal depression, which it certainly did, remembering that what it replaced was deep anaesthesia with a single inhalational agent given with a facemask. Hardly a contest! But what everyone (including me at the time) forgot was that the vast majority of babies given the rotten old anaesthesia, perversely came to no great harm and the mothers did not succumb to torrential bleeding from the relaxed uterus. Certainly the neonates were sleepier, but virtually none would have come to grief with modern resuscitation. If we had been honest, the attraction of the new method was the speed and ease with which we could present the intubated paralysed mother to the obstetrician, but this was not a particularly altruistic motive, and we talked inordinately about fetal depression, totally confusing a low Apgar score due to deep anaesthesia (not

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dangerous) with a similar score due to asphyxia (Signifi cantly dangerous). We did not advertise the increased incidence of death due to Mendelson's syndrome and failed intubation resulting from suxamethonium and crash induction. This required the Confidential Enquiry into Maternal Deaths to bring it to our attention.

Why is it that we extrapolate 'deep anaesthesia is bad' to 'any anaesthesia is still a little bit bad'? Yet we laugh at patients who say 'If one pill does me good, 10 will do me 10 times as much good'.

The concept of a 'rigid protocol' makes me shudder. Where did the 'art of anaesthesia' go? If the specialty teaches you nothing else, it teaches you about individual variation and the need to respond to obvious signs that the anaesthesia may be too light.

It is to be applauded that in Leeds one may now use up to 500 mg of thiopentone for induction, but why is the isoflurane reduced after delivery? Is the patient less likely to awaken? Surely nobody still believes that halothane 0.5% or isoflurane 1% will cause dangerous uterine bleeding. (I have even heard it advanced that such a potent concentration could significantly depress the left ventricular function in a case of mild pre-eclampsia!). Yet time and again one sees the volatile agent being switched off at delivery and a small dose of opioid substituted, albeit with some subtle adjustment of the nitrous oxide concentration. Why do we construct these convoluted protocols which have no advantage and merely increase the possibility of the mother waking up, or, all too often, remembering the last half of the operation as well as the first?

The Leeds workers have at least reduced their incidence of awareness by 75% and, maybe, looking at 1989, to zero; 0.4% sounds pretty reasonable, but this means in the UK where about 100 000 Caesarean sections are performed annually, that with, say, a 50% general anaesthesia rate, some 200 mothers will have an unpleasant experience and keep many lawyers happy. It would only take another wee turn of the vaporizer control.

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D.B. Scott

A personal view of postdural puncture headache

I have recently suffered a postdural puncture headache following an elective Caesarean section and would like to present an 'informed' patient's view.

The spinal was performed using a 27 gauge needle and involved only one dural puncture. The headache appeared at 24 hours on mobilisation, had typical features of a postspinal headache and was initially treated by bed rest, simple analgesics and fluids. By 48 hours I could not lift my head up without experiencing vice-like pain in my head and neck accompanied by nausea and sweating. Simple analgesics were totally ineffective. A blood patch was performed at 54 hours using 19 ml of autologous blood, and in itself caused pain in my back radiating down my left leg, and paraesthesia for several hours afterwards. It resulted in complete relief of symptoms but the headache recurred, albeit in milder form, 72 hours later following discharge. This was treated with bed-rest at home and resolved by the 12th postoperative day. Had I not experienced the postspinal headache, I would have been fully mobile within 24 hours. I was nursed flat for 24 hours by the midwives (despite the fact this is no longer policy in our hospital, in the light of evidence that it has no effect on the incidence of postspinal headache).[1,2] Immediately following the Caesarean section I was attempting to establish breastfeeding and I found this was hampered by having to lie flat, both initially and when on bed-rest for the headache.

I was unable to care for my baby adequately which distressed me and increased considerably the workload of the midwives on the ward. Since my return to work, I have spoken to several other mothers who have experienced a postspinal headache and they have expressed similar views on the effect of the headache on their relationships with their babies. Treatment of the headache with an epidural blood patch, although effective in 98% of cases,[3] is unpleasant and has (rarely) been associated with complications.[4,5]

In the light of my own experience, I applaud the attempts to reduce the incidence of postspinal headache in obstetrics by using alternative needles. However, in a study using 30 gauge needles,[6] although there were no postspinal headaches, there was a 25% failure rate attributed to increased technical difficulty. Cesarini *et al.*[7] also reported on postspinal headaches in 55 patients following spinal anaesthesia using the 24 gauge Sprotte needle and the preliminary report using the 26 gauge pencil point needle for combined spinal-epidural anaesthesia is equally encouraging, although numbers of patients studied are still small.[8] I await the result of the full study with interest.

In the meantime, in my clinical practice of elective obstetric cases, I would be unhappy to accept even a 1% incidence of postspinal headache, as I feel that one affected patient pays a high price in terms of the mother–child relationship in the all important first few days of the baby's life. A major advantage of a spinal is speed of onset, which is predominantly an advantage for the anaesthetist and surgeon. I now favour an epidural and use the time in establishing a block for the procedure to form a closer doctor–patient relationship. In the patients who do suffer a postdural puncture headache, I would advocate aggressive management with an early epidural blood patch to return mobility to normal as quickly as possible.

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Fault with an Ohmeda Excel 410 machine

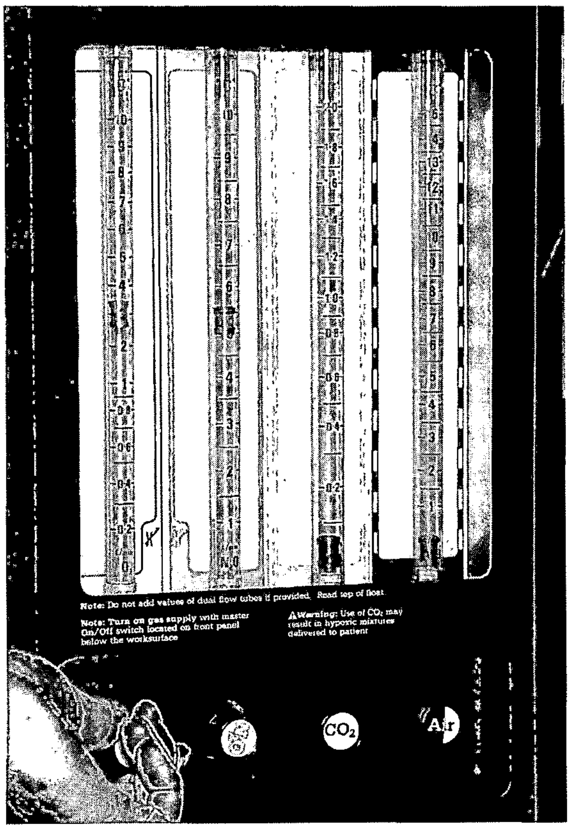

Fig. 1.

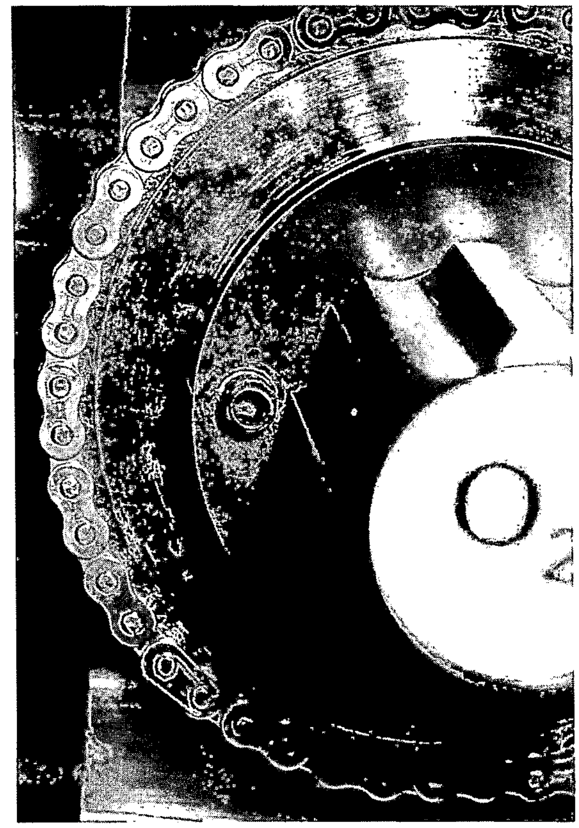

Fig. 2.

I wish to report a serious malfunction of an Ohmeda Excel 410 anaesthetic machine. The machine, which had been functioning normally, was taken out of use for a routine service by the manufacturers. It was then returned to the operating theatre and a few hours later was checked prior to use, following the guidelines of the Association of Anaesthetists. However, rotation of the oxygen flow control valve knob resulted in the situation shown in Figure 1. It was impossible to turn the oxygen flow control without the nitrous oxide control also turning; the highest oxygen concentration obtainable was 50%. The machine was removed from the operating theatre and the hospital equipment unit and the manufacturers informed.

The oxygen and nitrous oxide valve control bodies on the Ohmeda Excel 410 are linked by a chain sitting on two sprockets at the back of the valve knobs. Thus, opening the nitrous oxide control valve will also activate the oxygen valve so that a hypoxic mixture cannot be delivered. The oxygen valve knob is connected to its sprocket by a grub screw (Fig. 2), which moves away from the sprocket whenever the oxygen alone is turned on. When the machine was examined by Ohmeda, this grub screw was found to be screwed in 'half a turn' too far. There was thus a tight connexion between the oxygen control knob and its sprocket which resulted in a permanent linkage of the two valve bodies.

This event re-emphasises the importance of checking equipment before us.

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G. Lohmann

A reply

We thank the editor for giving us the opportunity to comment on the letter by Dr G. Lohmann. Representatives of Ohmeda, with members of the hospital staff present, examined the Excel 410 Anaesthesia machine and can confirm the presence of a problem as described by the hospital. In order to minimise the possibility of this matter arising again we are reviewing our engineer training procedures and we fully endorse the comments made with respect to the checking of anaesthesia machines prior to their use.

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P. Sim

Vaporizers — serviced and checked?

A 26-year-old woman presented for surgical repair of an ischial pressure sore and abscess. She suffered from lumbar spina bifida and was wheelchair bound. At the preoperative visit, she was found to be in good health with a normal cardiorespiratory system and no signs of autonomic neuropathy. The anaesthetic machine setup followed our normal practice of having both an enflurane and isoflurane vaporizer mounted on the backbar. Following a standard induction, the patient's lungs were ventilated with nitrous oxide, oxygen and enflurane, 70:30% and 0.8% respectively.

The first 15 minutes of the procedure were

unremarkable. She then became moderately hypotensive, with an arterial blood pressure of 75/40 mmHg. Rapid infusion of 500 ml Hartmann's solution corrected the blood pressure for 5–10 minutes, but despite normovolaemia and a good position, her systolic blood pressure remained between 70 and 80 mmHg systolic. The enflurane was turned off and she appeared to be well anaesthetised for the remaining 45 minutes of the procedure. Following reversal of neuromuscular blockade, spontaneous respiration returned promptly. However, she remained deeply anaesthetised. She was disconnected from the anaesthetic machine, which was supplying 8 litres/minute oxygen. It was immediately apparent that there was a considerable amount of vapour issuing from the anaesthetic machine, despite both vaporizers being turned off. The patient was taken to the recovery room, where she was extubated, awake, 40 minutes later.

Both vaporizers, Ohmeda Mk III Enfluratec and Fortec, were then tested separately with a Bruel and Kjaer gas monitor with 6 litres of oxygen flowing through the anaesthetic machine. The Enfluratec was normal. The isoflurane vaporizers gave the following readings:

Dial position	Percentage isoflurane 6 litres/minute oxygen
Off	1.5%
0%	3.0%
1%	4.5%
3%	Unrecordable, > than 5%

The vaporizer had just been returned from service at Ohmeda. The Department of Health and Ohmeda were both immediately informed by letter. A separate independent spectroscopic test was performed which confirmed that the vaporizer was giving widely inaccurate outputs, although different to those we had measured (Fig. 1).

Following discussions with Ohmeda, the name plate and control dial were removed from the vaporizer (Fig. 2). It was instantly obvious that the Woodruff key which connects the dial to the central spindle was misplaced, and that this was the cause of the malfunction. The difference between the results would readily be explained by the dial slipping freely on its spindle. When the Woodruff key was replaced, the vaporizer functioned normally.

Several issues are raised by this report. Firstly, that a check on vapour concentration should be considered as part of a pre-operative machine check, which has implications for the clinical availability of vapour analysers. Secondly, a calibration check should perhaps be part of the service of anaesthetic equipment: at present, service engineers make only a physical check of connexions, with no calibration check. Thirdly, we would recommend modernising the design of the spindle-dial Woodruff key locking mechanism on this widely used

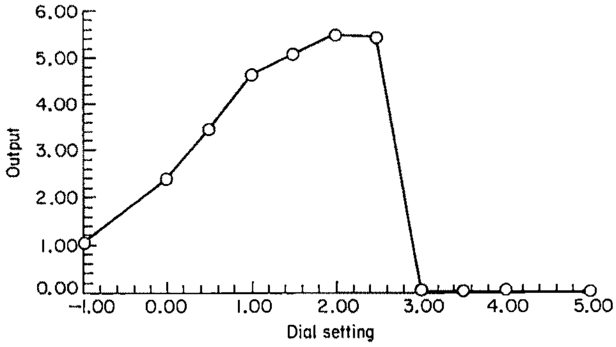

Fig. 1. Vaporizer output (isoflurane vaporizer BBTQ 03657).

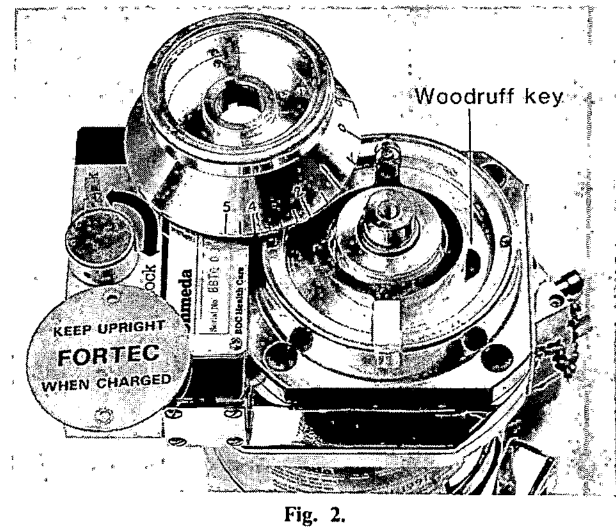

Fig. 2.

vaporizer to prevent recurrence, since this problem has occurred before.

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A reply

Thank you for giving us the opportunity to comment on the above letter. Since we have not yet been given the opportunity to examine the vaporizer in question our response is based purely upon Dr Lack's comments and simulation testing performed at our facility in Steeton, West Yorkshire. We are obviously disappointed that the vaporizer had been partially dismantled by the hospital. We would have liked the opportunity to measure the delivered concentrations from the vaporizer in the exact condition that it was in when Dr Lack experienced the reported problem. It is possible that the key could have been dislodged when the dial was removed. However, the performance described could be explained by the incorrect location of the Woodruff key, which locates the dial on the valve.

In attempting to simulate the condition described we removed the Woodruff key from an Isotec 3 vaporizer and orientated the control valve so that with the dial at the 'off' position the vaporizer delivered 1%, as in the graph of results from the spectroscopic test provided. We subsequently measured the output at all dial settings and recorded the following results:

Dial setting	Delivered concentration of isoflurane
'0'	2.07%
1	4.24%
2	4.88%
3	0
4	0
5	0

As can be seen from the above the Tec vaporizers are designed so that the valve will not deliver significantly more than the expected maximum of 5% anaesthetic agent if it is incorrectly positioned.

We have reviewed our vaporizer service procedures and acknowledge that it may be possible for the key to become dislodged when the dial is fitted. It is, however, a feature of our service training that a visual confirmation of the correct seating of the key is made. Beyond this the vaporizers are of course subjected to stringent performance tests at various flows and temperatures. We can only suspect that the person who fitted the dial may not have

identified that the key had moved. The screw which secures the dial to the valve could have been sufficiently tight to prevent it moving out of its correct position throughout our manufacturing tests and its initial period of use.

Since we have been manufacturing the Tec 3 for 23 years with only one similar recorded occurrence we believe that the design is well proven. We have, however, performed refresher training of our service technicians to re-emphasise the importance of this operation and are currently reviewing our quality assurance procedures.

With regard to your comments on pre-operative checks, Ohmeda fully supports the use of reliable monitors to provide early warning of undesirable situations.

Once again, may we thank you for giving us the opportunity to comment on the letter. If you require any further information please do not hesitate to contact us.

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The oesophageal detector device

The oesophageal detector device using a syringe[1] or a self-inflating bulb[2] has been shown reliably to distinguish oesophageal from tracheal tube placement in both children[3] and adults.[1,2] However, the device failed to confirm tracheal intubation in three adult patients with airway obstruction. The first patient had a large thyroid compressing the trachea and was scheduled for subtotal thyroidectomy; the second was an asthmatic who was scheduled for laparotomy; the third, a suspected case of lymphoma, was scheduled for diagnostic biopsy; she had large matted masses in the anterior mediastinum compressing the trachea with complete opacification of the left hemithorax and lower right hemithorax. In the three patients, general anaesthesia was induced with thiopentone and suxamethonium and orotracheal intubation was performed. Applying the squeezed bulb to the adaptor of the tracheal tube was not followed by refilling in the first patient and refilled very slowly in the other two patients. Laryngoscopy confirmed the proper positioning of the tracheal tube in all patients.

The principle underlying the oesophageal detector device is that the trachea is held open by rigid cartilaginous rings to allow free aspiration of the gas within the respiratory tract, while the oesophagus is not supported and collapses when a subatmospheric pressure is applied within its lumen.[1] The device may fail to confirm tracheal intubation in patients with tracheal obstruction or tracheomalacia, as well as in asthmatics, and the incidence of failure may increase in patients with low lung compliance. The device may also fail in children under one year, since the tracheal wall is not held rigidly open by cartilage as in older children and adults.[4]

It may be concluded that the oesophageal detector device may fail to confirm correct tracheal tube placment in patients with upper or lower airway obstruction and in patients with low lung compliance. Equivocal results may also occur if the tracheal tube itself is kinked or blocked.[5]

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Blood pressure recording during carotid endarterectomy

We wish to report the following incident which occurred during anaesthesia for carotid artery surgery.

A 50-year-old man with a history of transient ischaemic attacks affecting the left side of the body presented for carotid endarterectomy. Carotid angiography demonstrated severe stenosis at the right carotid bifurcation, but no significant disease further proximally in the common carotid artery. Before anaesthesia, monitoring was established with ECG, pulse oximetry, noninvasive blood pressure (Dinamap) on the right arm, and invasive blood pressure from the left arm; recordings from the two methods correlated well both before and after induction of anaesthesia and positioning of the patient for surgery. During surgery a T-shunt (Inahara Pruitt Inlying Shunt) with a body size of 9 Fr and a common carotid balloon capacity of 1.5 ml was inserted via an arteriotomy of the right carotid bifurcation, and the balloon inflated. It was soon realised that the blood pressure recorded by the Dinamap on the right arm was significantly lower (80/60 mmHg) than that recorded from the left radial arterial line (140/80 mmHg). Two further Dinamap readings confirmed the discrepancy. The patient's right radial pulse could not be palpated. On deflating the common carotid balloon of the T-shunt, there was immediate restoration of the pulse and agreement of the indirectly and directly recorded blood pressures. On closer examination it was apparent that the T-shunt moved 2–3 mm proximally whenever the common carotid balloon was inflated. This, presumably, caused the balloon to draw itself into a position at the bifurcation of the brachiocephalic artery and thus partially occlude the right subclavian artery at its origin.

The balloon was left partially deflated and surgery proceeded uneventfully. There were no permanent sequelae. While it is important to monitor arterial pressure in the contralateral arm in patients undergoing carotid artery surgery, this incident illustrates the need also to monitor the circulation to the ipsilateral arm in order that such episodes as this do not go undetected.

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Cardiorespiratory effects during gastrointestinal endoscopy

We wish to add our comments to those of Murray *et al.* (*Anaesthesia* 1991; **46:** 181–4) regarding the adverse cardiorespiratory effects during gastrointestinal endoscopy. The authors report that endoscopy causes hypoxia (oxygen saturation < 90%) and that the level of hypoxia closely correlates with electrocardiographic S-T segment depression. The study poses three important clinical questions; does the adjunctive use of opioids with benzodiazepines deleteriously affect oxygen saturation?; can hypoxia be reversed with supplementary intranasal oxygen?; and if so, can prophylactic intranasal oxygen therapy prevent hypoxia during endoscopy?

We have shown previously that the decrease in oxygen saturation during colonoscopy in 76 patients occurs to a similar degree with equipotent doses of diazepam (as Diazemuls) or midazolam alone and also with the combination of diazepam with pethidine and midazolam with pethidine.[1] Hypoxia occurred in 53% patients (oxygen saturation < 90%) and in all cases oxygen saturation was corrected to baseline levels with 4 litres/minute of intranasal oxygen. Diazepam was preferable to the other three regimens because it caused a significantly smaller decrease in the systolic and diastolic blood pressures.

We recently assessed 100 patients undergoing upper gastrointestinal endoscopy in a randomised study using two sedative regimens; diazepam 6 mg (range 2–10), or diazepam 12 mg (range 8–20).[2] Oxygen at 4 litres/minute was given via the nasal route prophylactically in 50% of the patients during endoscopy. There was no statistical difference between the oxygen saturation levels in patients receiving the two drug regimens. However, the group who received prophylactic oxygen had a mean nadir oxygen saturation of 98% (95% confidence intervals 97–99%) compared with a mean nadir of 93% (92–94%) ($p < 0.01$). In the latter group of 50 patients without prophylactic oxygen, 11 patients became significantly hypoxic (oxygen saturation 80–89%). None of the patients with prophylactic oxygen suffered from hypoxia.

We believe that all patients should be given prophylactic oxygen therapy during upper gastrointestinal endoscopy and colonoscopy. The cost of the piped oxygen and nasal canula amounts to less than 90 p per patient, so that the cost of providing patients with prophylactic oxygen represents < 1% of the cost of an endoscopic procedure.

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J. Colvin

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Nitrous oxide and laparoscopy

The article on the implications of the use of laser surgery during laparoscopic cholecystectomy (*Anaesthesia* 1990; **45:** 944–5) surprises me, in that it never mentions the problem of the use of nitrous oxide during this procedure. As anaesthetists are aware, and as Eger and Saidman[1] showed, the intestinal gas volume in dogs increases by 100–200% during a 4 hour administration of nitrous oxide and this distension lasts well into the postoperative period. Of course, passing a nasogastric tube usually gives good operating conditions, but would it not be appropriate to suggest, or mention, total intravenous anaesthesia in order to give the surgeon optimal conditions for laparoscopy. Optimal conditions in return will make the potentially enormous impact of laser use on a district general hospital lighter.

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A reply

Thank you for giving us the opportunity to reply to Dr Verheecke's letter. We agree that a total intravenous technique may be an alternative. However, this was the first documented case, since when over 100 cases have been performed. Increase in intestinal gas volume has not been a problem to the surgeons despite our use of nitrous oxide in all cases. It is the introduction of new technology and developing surgical techniques with which the anaesthetist must be familiar, rather than the precise mode of anaesthesia that causes the impact on a district general hospital.

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E.A.F. Clements

Anaesthesia for adults with congenital heart disease

We were interested to read the case report of anaesthesia for eye surgery in an adult patient with congenital heart disease (*Anaesthesia* 1991; **46:** 122–3). We wish to describe the management of a similar patient where a successful outcome was achieved with more conventional drugs.

A mentally retarded 27-year-old woman with congenital rubella syndrome required enucleation of her right eye. Her cardiac abnormalities were hypoplastic pulmonary arteries, a right to left shunt at atrial level, tricuspid regurgitation and an underdeveloped right ventricle. A pulmonary

valvotomy had been performed at 9 months of age. She was not in heart failure and took no cardiac medication but she was cyanosed and her exercise tolerance was limited to shuffling a few steps. Investigations showed blood pressure was 120/80 mmHg, ECG sinus rhythm at 80/minute, right ventricular hypertrophy and right bundle branch block. Haemoglobin was 17.8 g/dlitre and oxygen saturation 85%. Total plasma CO_2 of 18 mmol/litre indicated a chronic metabolic acidosis.

Her mental condition and fear of needles precluded local anaesthesia. Because of the considerable risks of general anaesthesia the operation was performed in the cardiac surgery operating theatre which had an adjacent intensive care unit. Premedication was with temazepam 10 mg and atropine 0.6 mg with topical EMLA cream to the proposed puncture sites. Cannulae were inserted into a right forearm vein and her right radial artery while she was breathing a 50:50 mixture of oxygen and nitrous oxide. After cannulation the arterial pressure was 100/65 mmHg, heart rate 90/minute and oxygen saturation 90%. Arterial blood sampling showed; H^+ 43.7 nmol/litre $P\text{O}_2$ 9.03 kPa, $P\text{CO}_2$ 3.28 kPa, K^+ 3.2 mmol/litre, HCO_3^- 13.7 mmol/litre standard base excess −10.7 mmol/litre. Under close monitoring small boluses of propofol and alfentanil were injected intravenously and repeated until the patient went to sleep (total doses, propofol 50 mg and alfentanil 250 μg). Suxamethonium 50 mg intravenously and lignocaine spray to the larynx preceded tracheal intubation. The patient's lungs were ventilated throughout the procedure with a mixture of 50% oxygen, nitrous oxide and up to 1% enflurane. Propofol 20 mg and alfentanil 250 μg were given before incision, but further muscle relaxation was not required. Arterial pressure remained between 80/50 and 90/60 mmHg with a pulse rate between 75 and 80/minute and oxygen saturation of 89–90%. Blood gas analysis after 20 minutes of anaesthesia showed: H^+ 51.6 nmol/litre, $P\text{O}_2$ 8.54 kPa, $P\text{CO}_2$ 4.03 kPa, K^+ 3.1 mmol/litre, HCO_3^- 14.1 mmol/litre, standard base excess −11.3 mmol/litre.

At the end of the 40 minute procedure her trachea was extubated while she breathed 1% enflurane in oxygen, and within 5 minutes she was in the adjacent intensive care unit breathing oxygen from a facemask. She was awake, alert with an arterial pressure of 140/85 mmHg, pulse rate of 100/minute and an oxygen saturation of 97%. She was pain free, not distressed and further analgesia was not required. Within 2 hours her oxygen saturation whilst breathing air was 88% and she returned to the ophthalmic unit.

We have used a similar technique during sterilisation of a 30-year-old patient with a univentricular heart and in both cases our patients were awake more rapidly than Riley and McBride's. We feel that this is a considerable advantage when dealing with this type of patient. Whatever type of drugs are used, however, it is the manner of administration that is paramount. Appropriate cardiovascular and respiratory monitoring should precede anaesthesia and be continued until full recovery has taken place. We cannot improve on the advice given in 1943 to restore the reputation of thiopentone following the disaster of Pearl Harbour: 'Small doses administered slowly with intervals between injections of sufficient length to allow the full effect to take place is the only rational method of administration'.[1] The same principles can of course be applied to the use of infusions.

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Pulmonary artery wedge pressure in ARDS

The results of the survey amongst British intensive care units on the measurement and the manipulation of pulmonary artery wedge pressure (PAWP) (*Anaesthesia* 1991; **46:** 160–1) are interesting, but perhaps not surprising. A so-called 'watershed' PAWP for distinguishing between high and low pressure pulmonary oedema will depend upon the degree of microvascular permeability, amongst other factors. It is not at all certain that the change in permeability of lung microvasculature in those affected by adult respiratory distress syndrome (ARDS) is uniform or that it does not vary during the course of the illness. It has recently been shown[1] that those patients who survive ARDS, when compared as a group with those who do not, are significantly less affected by changes in permeability. The level of serum albumin is another major influence on the tendency to oedema formation and this value is often depressed in the critically ill patient.[2] Correspondingly, there must be uncertainty about a watershed PAWP.

To some extent the spectrum of opinion revealed by the survey may also reflect the fact there is no optimal treatments for ARDS. The conflicting aims of keeping PAWP low and maintaining or even augmenting forward flow represent the central dilemma in the management of this condition. As the authors observe, the therapeutic trade-off between a deliberate reduction of PAWP and the resultant fall in cardiac output (and oxygen delivery) is highly questionable.

There is no firm evidence [3,4] to support the notion that pulmonary artery catheterisation and the measurements permitted by this technique have improved outcome in ARDS or any other critical illness. The suggestion by McQuillan and Young of a systematic prospective study, to evaluate the efficacy (or otherwise) of purposefully lowering PAWP in ARDS is therefore to be welcomed.

However, the key to a reduction of the high mortality associated with ARDS seems unlikely to lie in the mere manipulation of cardiorespiratory variables. The focus is shifting to the fundamental pathophysiology underlying the manifestations of this syndrome.[5,6] Successful intervention will require a more coordinated approach between supportive therapy and the use of specific pharmacological agents designed to target the many cellular and humoral mediators implicated.

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Foreign body in a laryngeal mask airway

We are grateful to Dr I.D. Conacher (*Anaesthesia* 1991; **46:** 164) both for his praise for this product and for drawing attention to a possible hazard, namely, that the plastic Luer valve in the inflation line may accidentally enter the airway tube if it becomes dislodged from its housing. This may occur during autoclaving due to the presence of air in the mask cuff. It is important that those who are responsible for autoclaving the laryngeal mask are made aware that the mask cuff must be completely evacuated immediately before autoclaving, to avoid pressure build-up forcing the valve out of its housing during the autoclave negative cycle.

Users should therefore always examine the inside of the tube carefully before use to ensure that it is free of any foreign material, as detailed in the Intavent Instruction Manual (second edition) under 'Device Performance Tests' — page 41.

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Postoperative oxygen via the laryngeal mask airway

Broadway and Royle have described the assembly of a Venturi T-piece system to supply supplementary oxygen to the laryngeal mask airway (LMA) (*Anaesthesia* 1990; **45:** 792–3). At newmarket Hospital the Portex Thermovent-T and Thermovent O_2 (Fig. 1) are routinely used to supply

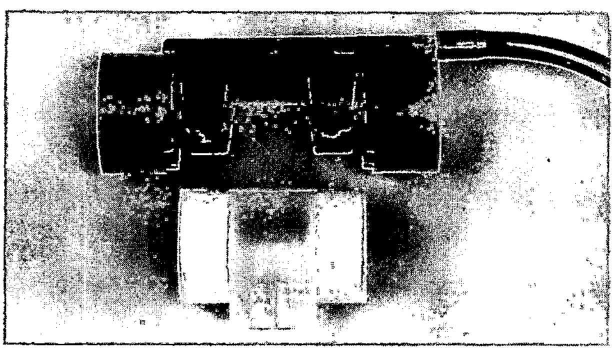
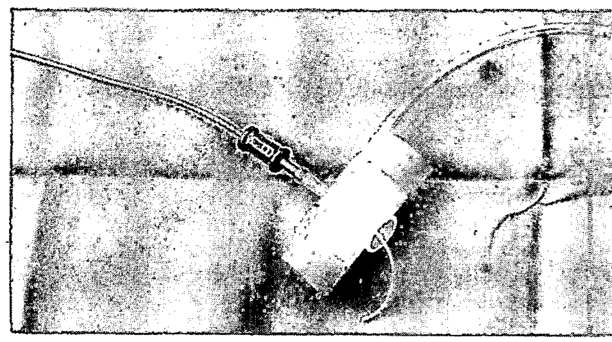


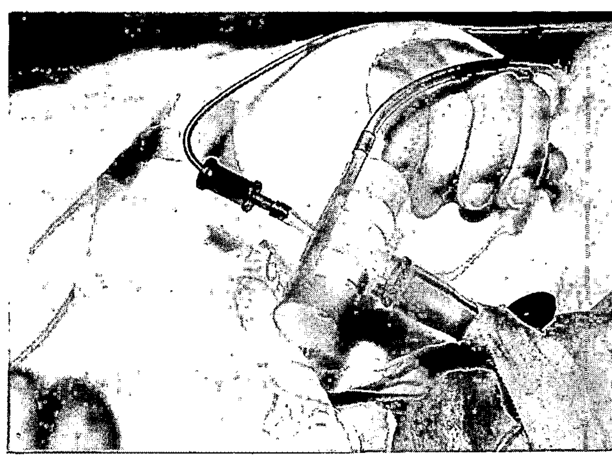
Fig. 1. The Portex Thermovent T and Thermovent O_2.

supplementary oxygen to the LMA during transport from the operating theatre to the recovery room and in the recovery room prior to its removal. The effectiveness of this method was assessed on 30 consecutive patients. Inspired oxygen concentrations were measured at differing oxygen flows using a specially adapted thermovent T and O_2 (Figs 2 and 3). Forty-five seconds were allowed at each flow, ranging from 1 to 8 litres/minute and increasing in 1 litre steps. Pulse oximetry was employed to ensure oxygen saturation remained above 97% and end-tidal carbon dioxide was monitored to exclude rebreathing. The results are shown in the Table and as expected the device functioned as a variable performance device with a degree of predictability.

Table 1. Mean inspired oxygen concentrations ($F\text{IO}_2$) of 30 patients receiving supplementary oxygen via the laryngeal mask airway, Portex Thermovent O_2 and Thermovent T at differing oxygen flows.

Oxygen flow (litres/minute)	Mean $F\text{IO}_2$	Standard deviation
1	26	1
2	32.6	4.5
3	36.8	5.2
4	41.3	3.7
5	43.5	4.2
6	47.4	4.3
7	51.4	4
8	51.4	2.5





Figs 2 and 3. The adapted Thermovent T and O_2.

Portex have described the use of the Thermovent T and Thermovent O_2 as an effective means of providing humidified oxygen enriched air to spontaneously breathing adults and children whose upper airways were bypassed by either a tracheal or tracheostomy tube, without adding significant resistance to breathing. It has now been shown that this system may equally well be used with the LMA. At set flows the Thermovent T and O_2 will supply predictable, reasonably accurate, inspired oxygen concentrations to patients recovering from general anaesthesia involving the laryngeal mask airway; this mode of administering oxygen postoperatively is convenient and effectively controls $F\text{IO}_2$ in the absence of rebreathing. Because the system operates via a single lightweight device, it offers a more flexible performance than the more cumbersome Venturi system reported by Broadway and Royle.

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Laryngeal mask airway for coronary artery bypass grafting

We were interested to read the report by White *et al.* *Anaesthesia* 1991; **46:** 234) describing the use of the laryngeal mask airway (LMA) for coronary artery bypass surgery in a patient whose trachea could not be intubated. We too have found the LMA useful in a similar case, but believe that the use of this device in cardiac anaesthesia deserves further comment.

In the case described by White *et al.* neuromuscular blockade was reversed at the end of the operation and the LMA was removed soon after. The question of postoperative management of the airway in the cardiac intensive therapy unit therefore did not arise. However, together with many others, it is our practice to mechanically ventilate the lungs for several hours after cardiopulmonary bypass; the patients tracheas are only extubated when they are haemodynamically stable, normothermic and awake.

In our case of unexpected difficult intubation prior to coronary artery surgery, we could not intubate the patient despite repeated attempts with conventional aids. A good airway was, however, successfully obtained when a LMA was inserted, and effective ventilation was achieved easily with no audible air leak. Despite this success, we chose not to continue with this method of airway management, because we were not confident that continued use of the LMA would reliably guarantee adequate ventilation throughout the intra-operative and postoperative periods. In particular, we felt unable to defend any decision to leave a patient whose airway was managed in this way in the care of ITU nurses who were unfamiliar with the device. We were also concerned that if, with further attempts, successful tracheal intubation were eventually to be achieved, the duty anaesthetist (and the patient) would be left in a disadvantaged position should this tube need to be urgently replaced at any time in the peri-operative period. We therefore chose to perform an elective tracheostomy before coronary artery surgery. The LMA was used for control of the airway and maintenance of anaesthesia whilst this procedure was carried out. The scheduled operation then took place uneventfully, and the patient made a good postoperative recovery.

Should we be faced with a similar situation in the future, we would manage it in the same way. We believe that the LMA is a satisfactory intra-operative alternative to a tracheal tube under certain circumstances, but we cannot recommend its use for mechanical ventilation in the intensive therapy unit. In addition, the LMA may be unsuitable for cardiac anaesthesia for other reasons. For example, the high inflation pressures, which are often used as part of 'de-airing' procedures could not be achieved with the LMA, with which air leaks commonly occur if inflation pressures much above 20 cmH_2O are used.

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Trainee anaesthetists and the laryngeal mask airway

At the recent 'Controversies in Obstetric Anaesthesia' symposium at the Royal College of Obstetricians and Gynaecologists, the general opinion seemed to be that the laryngeal mask airway (LMA) might be a useful aid in airway maintainance following failed intubation at induction of general anaesthesia for Caesarean section, provided that the anaesthetist was experienced in its use. With the increasing availability and popularity of the LMA, it is clear that a great number of anaesthetists, including trainees, are gaining a degree of expertise in its use, mainly during procedures lasting more than a few minutes and with spontaneous respiration. In many centres use of the laryngeal mask has become almost routine for such cases.

It is, however, considered vital that during routine anaesthesia the new generation of trainees are still taught and actively encouraged to manage the airway in the traditional manner with mask and oropharyngeal airway, even in the case of the difficult airway or longer procedures where the temptation may well be to seek the 'easy' option and use a laryngeal mask. Patients for emergency Caesarean section are nearly always anaesthetised by trainees, often during the night and should it prove impossible to intubate the trachea, successful insertion of the laryngeal mask is not guaranteed. Maintainance of oxygenation without aspiration is clearly vital, and it may be necessary to continue under inhalational anaesthesia using a facemask and the oropharyngeal airway.

It is hoped that the ability of the next generation of anaesthetists to maintain the airway for prolonged periods or in difficult circumstances does not suffer due to increased use of the LMA during routine anaesthesia.

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The laryngeal mask and the oesophagus

The laryngeal mask (LM) should not be used where there is a known danger of aspiration of gastric contents, unless tracheal intubation has failed. There are some occasions when regurgitation occurs quite unexpectedly, however. As the laryngeal mask offers such a different approach to management of the airway, it is legitimate to ask whether we have formulated the best way of dealing with regurgitation when it occurs with the LM *in situ* and whether the conduct of anaesthesia might have any influence on its incidence.

In my own practice, four cases of unexpected regurgitation occurred during spontaneous breathing of anaesthesia (as opposed to during recovery) using laryngeal mask prototypes between 1981 and 1987. In each case, liquid was seen passing up the tube from the mask. My reaction, rightly or wrongly, was as follows: first, to tilt the patient into the Trendelenburg position while informing the surgeon; second to increase the F_{IO_2} to 100%; and third, to deepen anaesthesia while controlling ventilation with gentle manual bag-squeezing. As soon as I was satisfied that oxygenation was being maintained, I performed suction through the tube of the LM and in two cases was able subsequently to use a fibrescope to examine the trachea directly through the LM. In one of these two cases bile

staining of the upper trachea was noted but the other was clear. All patients received intravenous dexamethasone while still under the anaesthetic. Auscultation of the lung fields in all patients remained clear throughout. No attempt was made to remove the LM, administer suxamethonium or intubate the trachea in any of the patients. All recovered normally, with normal postoperative chest X rays.

An additional case, resembling that described by Koehli[1] occurred while I was demonstrating an early commercial LM for a cholecystectomy in a short, obese woman (a patient in whom I would now no longer use it). Left-sided bronchial spasm was noted fibrescopically after facemask, laryngeal mask and finally tracheal tube ventilation had all been found difficult. Interestingly, an 8-mm tracheal tube had been passed into the oesophagus after LM insertion to demonstrate the feasability of the technique. A gastric tube was passed down this into the stomach, which was found to be empty, prior to starting surgery. It seemed possible, in retrospect, that the patient had aspirated on induction while breathing against a partially obstructed upper airway. A bile-stained mucous plug was expectorated on the second postoperative day; the patient recovered fully.

If there is evidence that regurgitation is occurring, it should be remembered that the mask serves to obliterate the space in the pharynx which would otherwise act as a reservoir for regurgitated fluid. Fluid entering the bowl of the LM is not 'directed preferentially' into the trachea as has been stated.[1,2] There is merely less of it to be aspirated at any given moment, because the pharyngeal reservoir has been filled by the inflated mask cuff. Moreover, fluid entering the bowl of the mask is free to escape up the tube during expiration, offering rapid visible evidence through the transparent tube wall. Suction should therefore be applied through the LM tube, not the pharynx.

The suggestion that regurgitation risks are lessened by removal of the mask in the operating theatre and placing the patient in the lateral position for transfer to recovery area[1] is not borne out by my own experience, in which removal has been carried out by trained recovery staff without serious mishap since 1982. However, regurgitation might be provoked by high intra-abdominal pressures resulting from spasmodic reaction to pain in the partially anaesthetised patient. This situation is commonly observed when patients are turned on their sides at the conclusion of surgery. Another possible cause of regurgitation is transmission of high negative intrathoracic pressures to the oesophagus if laryngeal spasm is provoked by surgical stimulation at inadequate levels of anaesthesia.

Adequate anaesthesia during surgery and avoidance of disturbing the patient during recovery are certainly fundamental to smooth, uneventful use of the LM. Might these factors not also be important in reducing the likelihood of unexpected regurgitation in the technically fasted patient?

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Intubation guide marks on tracheal tubes

Dr Mehta has pursued in depth (*Anaesthesia* 1991, **46:** 306–8) an idea that was investigated and reported for use on both adult and paediatric tracheal tubes 21 years ago.[1] In that study, marker rings were placed 1 cm from the upper end of the cuff on adult tubes, and at 1 cm intervals from the tip of noncuffed paediatric tubes. Dr Mehta's study clearly justifies the need for a gap of at least 2 cm between cuff margin and vocal cords on cuffed adult tubes. Hence, placing the guide mark at 3 cm, as on current Portex adult cuffed tubes, is ideal. In 1970 the use of polyvinyl chloride tubes was confined to intensive care, and the dominant manufacturer, Portex, said that printing marker rings would be technically difficult. However, Franklin, suppliers of the marked red rubber tubes used in the 1970 tests and illustrated in the *Lancet* article, said production would be feasible but would double costs.

As a result of improvements in manufacturing technique marker rings have been added in recent years to increasing types of tracheal tube where they sometimes provide valuable help.

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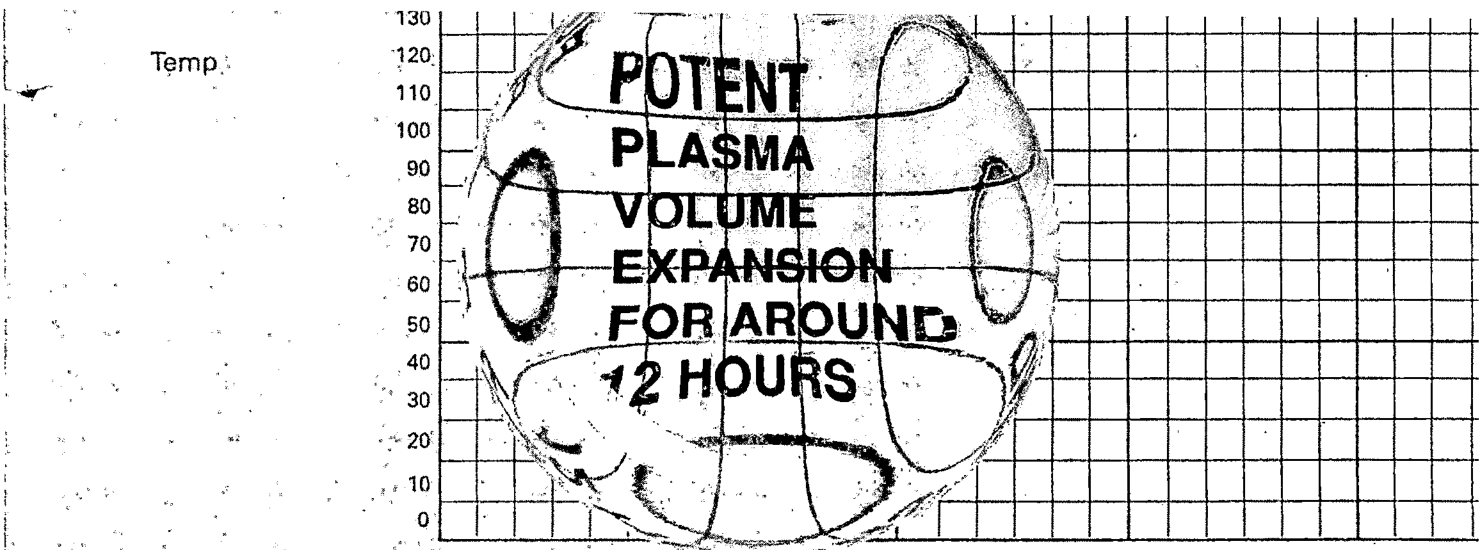
Children's fingers and spurious pulse oximetry

I would like to report an incident where a falsely low oxygen saturation (Spo_2) was recorded by the Hewlett Packard 78354A oximeter using the M1190A finger probe. A healthy 4-year-old scheduled for orchidopexy was premedicated with temazepam, metoclopramide and EMLA cream. Anaesthesia was induced with propofol 2.5 mg/kg and maintained with oxygen 1 litre and nitrous oxide, 2 litres/minute respectively, and 2% isoflurane with spontaneous ventilation through a Mapleson F circuit and mask. An ilio-inguinal/hypogastric block was performed using 6 ml of plain 0.25% bupivacaine. During this time clinical observations were satisfactory and ECG indicated sinus rhythm of 120/minute.

After transfer to the operating theatre, recordings indicated a blood pressure of 95/50 mmHg, heart rate of 110/minute, but an Spo_2 of only 92% despite good peripheral perfusion and adequate respirations at 18/minute. Oxygen was increased to 50%, but over the next 5 minutes the Spo_2 decreased to 87% despite otherwise satisfactory observations. The child's left arm was positioned horizontally on the table at his side with the oximeter probe on the index finger. The arm was not compressed in any way and the plethysmograph signal looked normal and indicated the same heart rate as the ECG. It was thought there could be optical interference due to the operating theatre lights illuminating the probe under the green surgical drapes and so the hand was brought up to lie on the chest. In doing so, it was noticed



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that the finger moved freely within the oximeter probe and the Spo_2 immediately indicated 99%. The remainder of the intra-operative course was uneventful, as was recovery.

The probe was examined to see if the erroneous result could be reproduced. A strong light was shone through the surgical drapes in order to mimic the scatter of green light. Green finger nail polish can produce an apparent decrease in saturation of as much as 5%,[1] but the Spo_2 in this case either remained at the steady state value or was not recorded due to interference and the 'SO_2 nonpulsatile' alarm would sound. However, when the finger was moved slightly to the side within the adult sized probe, a reduction of Spo_2 did occur from 99% to 92%. This finding agrees with the report of the 'penumbra effect,' where displacement of the probe and finger can cause a spuriously low Spo_2.[2]

This report highlights the fact that a child's small finger can easily move about within a preformed adult sized probe and lead to malposition. It should be considered early in the presence of mild desaturation since it is easily detected and corrected.

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Prilocaine associated methaemoglobinaemia and the pulse oximeter

Pulse oximetry has had an important impact on the practice of anaesthesia, although the reliability of the readings may be a problem. Their design has therefore been modified to reduce artifactual errors, for example, averaging samples over short periods of time to reduce motion artifact. The majority of errors, however, occur at the patient-probe connexion or from within the patient. The classification of artifacts has been documented previously.[1] The oximetry findings of an interesting case are presented.

A 47-year-old, 62 kg, hypertensive female with chronic renal failure was scheduled for a revision of her arterio-venous fistula. Pre-operatively her fluid balance was satis factory, and her blood pressure was well controlled with nifedepine 10 mg twice daily. Investigations revealed haemoglobin 10.6 g/dlitre, sodium 140 mmol/litre, potassium 5.9 mmol/litre, urea 30.7 mmol/litre and creatinine 1076 mmol/litre. Premedication consisted of temazepam 20 mg orally one hour pre-operatively. A perivascular axillary brachial plexus block[2] was performed with 50 ml 1% plain prilocaine. After 45 minutes there was no evidence of any block. An alternative approach via the interscalene route was therefore performed[3] and 10 ml of 1% prilocaine with 10 ml of 0.5% bupivicaine was injected. Twenty minutes later there was a partial sensory block, a sympathetic block, and an ipsilateral Horner's syndrome. The block was therefore supplemented with local infiltration of the forearm with 10 ml of plain 0.25% bupivicaine.

Just after surgery had begun, it was noted that the patient had become dusky with the pulse oximeter showing a saturation of 75%. The patient remained comfortable and orientated, with no change in her respiratory or cardiovascular parameters. Prilocaine-induced methaemoglobineamia was suspected. Saturations remained between 75 and 77% despite 50% inspired oxygen. Arterial blood gases taken before oxygen administration revealed a Pao_2 of 10.6 kPa, $Paco_2$ 4.7 kPa, the base excess -1.5 mmol/litre with a derived oxygen saturation of 96%. Samples were also taken for methaeoglobin and prilocaine levels.

Methylene blue 30 mg was administered intravenously and within 5 minutes the oxygen saturations had risen to 87%. Following a further 30 mg the saturation rose to 91%, finally reaching 93% 10 minutes later. Supplementary oxygen was continued until the procedure had finished and the patient was in recovery. The methaemoglobin level measured by an IL-282 cooximeter was found to be 6.6%. Normally methaemoglobin levels are less than 1% and levels greater than 10% are clinically significant.[4] The prilocaine level in this patient was 1.43 μg/ml, toxic symptoms occur when plasma levels are greater than 5 μg/ml.[5]

Intravenous dyes can cause transient, apparent desaturations which return to baseline within 5 minutes.[6] In this patient intravenous methylene blue resulted in an increase in oxygen saturation due to reduction of the oxidised ferric iron molecule in the haemoglobin to the ferrous state. Consequently the proportion of light absorbed by normal haemoglobin and that by methaemoglobin altered. This change resulted in a rise in oxygen saturation. Methaemoglobinaemia in anaemic patients is potentially more serious than in normal patients, as there are then two factors operating to reduce oxygen content.[7] The total dose of prilocaine administered shows good correlation with the degree of methaemoglobinaemia. Methaemoglobin levels remain elevated after prilocaine administration for 6–8 hours.[8]

This case illustrates how useful pulse oximetry can be in managing patients requiring regional anaesthetic blocks. The development of prilocaine-induced methaemoglobinaemia in anaemic patients can have serious effects on oxygen delivery. We recommend the use of pulse oximetry in patients receiving large doses of prilocaine, especially if anaemic.

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Scavenging in the operating theatre

BS 6834: 1987 deals with safety and performance of anaesthetic gas scavenging systems. Drs Amoroso's and Sale's device (*Anaesthesia* 1991; **46:** 159) totally bridge the British Standard and can result in serious consequences.

Hospitals should be vigilant and disallow the use of DIY equipment noncompliant with current British Standards.

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Recurrent pleural effusions following superior vena cava thrombosis

I wish to report an unusual complication following cannulation of the external jugular vein. A 2.99 kg male infant was transferred to our care 72 hours after birth. He required fluid resuscitation and following this a transverse loop colostomy was performed for toxic Hirschsprung's enterocolitis. Postoperatively, he became septicaemic and scleraemic in appearance and great difficulty was experienced in gaining intravenous access. Finally, a 22 gauge teflon cannula was inserted into the right external jugular vein. Four days after this he developed the typical picture of superior vena cava (SVC) obstruction, and the cannula was removed. The presence of a thrombus in the SVC and collateral flow was subsequently demonstrated by a radioisotope venogram. The obstruction did not improve and 2 days later fluid was noted in the pleural cavities on radiological examination. The effusions required bilateral chest drains. They were of a staw-coloured transudative nature and never chylous, even after nasogastric feeding. Daily losses were often massive (up to 700–800 ml/24 hours). The child's condition steadily deteriorated and he eventually died aged 3 months. Postmortem examination confirmed SVC thrombosis and a *Pseudomonas aeruginosa* septicaemia.

Superior vena cava obstruction is a major danger of indwelling central venous catheterisation especially in the presence of increased blood viscosity. Mollitt and Golladay[1] reported a 7% incidence of SVC obstruction in children under one year of age with indwelling central venous lines. The occurrence of SVC obstruction in association with a cannula in an external jugular vein has not been reported as yet.

The complication of recurrent massive pleural effusions has been documented in children, but is not well known.[2] In a series of five preterm babies who developed recurrent transudative effusions as a result of SVC thrombosis from indwelling paediatric Broviac catheters, three died.[3] These effusions did, however, beccome chylous on enteral feeding. The development of recurrent chylous effusions is probably due to occlusion of the thoracic and right lymphatic ducts with resultant stasis within the pleural and pulmonary lymphatics causing pulmonary lymphangiectasia. The fact that the effusions are not always chylous reflects the usual state of enteral nutrition. The aetiology of the massive pleural effusions which occured in our case remains to some extent uncertain. However, the most likely explanation probably involves a similar mechanism to the formation of the chylous effusions mentioned above, despite our failure to demonstrate chyle on enteral feeding.

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Withdrawal syndrome after propofol

Experience locally with the use of propofol as an anticonvulsant agent and for short-and long-term sedation in patients, young and old, undergoing intensive care, parallels that of Grant and Worsley (*Anaesthesia* 1991; **46:** 238). Despite there being no product licence for its use in children, the quality of sedation produced is such that it has become the agent of choice here and in other Intensive Care Units.[1]

Although there have been no instances of convulsions following discontinuation of propofol infusions used for sedation, one recent case is of note. The patient, a previously fit 18-month-old girl, required ventilatory support after sustaining 20 percent burns and smoke inhalation in a house fire. For a 2-week period the child was sedated with a continuous propofol infusion. Upon cessation of the drug, extreme 'jitteryness' in the form of generalised twitching was noted. This gradually subsided over a period of 3 days. Blood gases and blood biochemistry during this time were normal and there was no suspicion of cerebral hypoxic damage as the child had been fully conscious on admission. Carboxyhaemoglobin levels at that time were only minimally raised.

In our view, the note of caution about the possibility of a propofol withdrawal syndrome, sounded by Au *et al.*[2] should be heeded.

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Propopol in myotonic dystrophy

A 37-year-old, slightly mentally retarded woman with Steinert myotonic dystrophy was admitted for cholecystectomy. Premedication consisted of midazolam 4 mg intramuscularly and 1 hour later an epidural catheter was inserted at the T_{10}–T_{11} interspace and 15 ml 0.5% bupivacaine injected. Ringer's lactate solution 500 ml and two doses of ephedrine 15 mg were required to maintain a normal arterial blood pressure. When the block was fixed and the haemodynamic status had stabilised, general anaesthesia was induced with propofol 2 mg/kg.

Immediately following the propofol injection myoclonic movements occurred in the extremities and appeared to provoke a myotonic state which began in the upper limbs and extended to the trunk. It was possible to intubate the trachea easily without muscle relaxants and the myotonia resolved with the introduction of isoflurane. Anaesthesia was maintained thereafter with isoflurane in 50% nitrous oxide and oxygen; the lungs were mechanically ventilated without the use of muscle relaxants. Recovery from anaesthesia was uneventful; analgesia was provided by an infusion of fentanyl into the epidural space.

Propofol has been used previously in a patient with myotonic dystrophy without a problem,[1] although in another case exaggerated physiological responses were reported.[2] In our patient, the myotonic response followed an episode of myoclonia and may have been due to a centrally mediated increase in muscle stimulation.

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Inadvertent dural puncture during caudal anaesthesia for Saethre–Chotzen syndrome

Dural puncture during caudal anaesthesia is rare. Two patients are presented that illustrate the importance of checking for the flow of cerebrospinal fluid (CSF) before injecting local anaesthetics.

Two siblings, aged 2 and 4 years, presented for day care surgery, one for orchidopexy and the other for repair of umbilical hernia. Both had been diagnosed as having Saethre–Chotzen syndrome, as had their mother and uncle. This is the most frequent of the acrocephalosyndactylies and is also the commonest inherited disorder that causes craniostenosis.[1] Surgery is often needed for correction of limb abnormalities. Intellect is low to normal. Anaesthesia was with propofol, atracurium and controlled ventilation with nitrous oxide, oxygen and halothane. Caudal injection was performed using an aseptic technique with a 21 gauge needle just through the sacrococcygeal membrane. In both cases a brisk flow of CSF was noticed immediately and the needle was removed. Anaesthesia and surgery proceeded uneventfully and rectal diclofenac was given for postoperative analgesia. The children were admitted overnight but neither developed postural headache. Early closure of the coronal suture may have lead to raised CSF pressure and the ballooning of the dura into the sacrum, although sacral prolongation of the dural sac is occasionally a normal variant.[2]

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Ginger as an antiemetic: possible side effects due to its thromboxane synthetase activity

The recent report that ginger root taken orally at the time of pre-operative medication significantly reduces postoperative emetic sequelae (*Anaesthesia* 1990; **45:** 669–71) must be tempered by the potent thromboxane synthetase inhibiting activity of ginger.[1] Our group has had extensive therapeutic experience with ginger. We have suggested numerous uses for it including preventing liver damage,[2] in burns,[3] in treating peptic ulceration,[4] as an antidepressant,[5] and in preventing aging penile vascular changes and impotence.[6] A word about side effects. We have carried out toxicological tests on ginger using the SOS Chromotest but could find no evidence of toxicity (unpublished observations). However, as a very powerful thromboxane synthetase inhibitor and prostacyclin agonist, ginger may have potent effects on bleeding time and on immunological parameters.

In summary, I think it may be wise to investigate changes in bleeding time before wholeheartedly recommending ginger root to prevent postoperative emetic sequelae.

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Masseter spasm in Williams syndrome

Drs Patel and Harrison (*Anaesthesia* 1991; **46:** 115–16) describe a case of masseter spasm when a 15 kg, 4-year-old boy with Williams syndrome was given two doses of suxamethonium 10 mg which were ineffective, and then 5 mg for tracheal intubation in the presence of laryngeal spasm. They do not find a convincing explanation and we would like to suggest one which we believe to be the cause.

The duration of the myotonic effect of suxamethonium, which may be interpreted as masseteric spasm, has been shown in adults to be significantly negatively correlated with dosage. The increase in tone lasted a mean of 27 seconds with 0.7 mg/kg of suxamethonium, but was prolonged to 50 seconds when the dose was reduced to 0.25 mg/kg.[1] The magnitude of the jaw tone showed no such correlation with dosage. The optimum conditions for intubation exist between the times to 95% block and to 5% recovery of the first twitch of the train of four.[2] Meakin *et al.*[3] have recently shown in children aged 1 to 7 years given 1 mg/kg of suxamethonium, that optimum conditions last less than 3 minutes on average, with a minimum of 1.7 minute. They state that their findings of a very brief recovery time using this dosage suggest that 'underdosage is the principal cause of the high incidence of 'masseter spasm' seen in some children's hospitals' and suggest the adoption of a dose of 2 mg/kg in children, which they found to last longer (> 5 minutes).

We conclude that in the child reported by Patel and Harrison, the low doses of suxamethonium used (0.66 mg/kg and 0.33 mg/kg) caused a prolonged increase in masseter tone, followed by a short period of relaxation, which was misinterpreted as masseter spasm.

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A reply

We would like to thank Drs Matthews and Vernon for their appraisal of our clinical problem. The highlighting of this aspect of the pharmacology of suxamethonium will require us to consider a change in our clinical practice.

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Airway management in patients with an end-tracheostomy stoma

We were interested to read the letter from Drs Northwood and Wade (*Anaesthesia* 1991; **46:** 319) describing the use of the Rendell–Baker Soucek mask for airway management, during induction and maintenance of anaesthesia, in patients with an end-tracheostomy stoma. We have also used paediatric facemasks in this situation and have found that the Laerdal infant mask with its more pliable edge provides a better gas tight seal, especially in lower stomas when the mask may impinge on the manubrium.

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Anaesthesia, 1991, Volume 46, page 707

Safety Action Bulletin

Hoskins Accident Trolley Cat No 3210: risk of collapsed backrest due to use of blind (pop) rivets SAB(91)20

The raised backrest of the above trolley collapsed when a sitting patient placed his weight on it. All these trolleys manufactured between January 1986 and July 1990 should be examined to see if the backrest is secured to the top of the trolley or the backrest height adjustment mechanism is held to the backrest using blind (pop) rivets. If so the trolley should be taken out of use and the manufacturer contacted to replace the rivets with nuts and screws.

Errata

Anaesthesia, 1991, Volume 46, pages 309–311

A comparison of lignocaine with prilocaine in axilliary brachial plexus anaesthesia

E.P. McCoy

Under the heading 'Nerve area' in Table 4 of the above paper the last item should read 'Medial cutaneous nerve of forearm'.

Under the *Acknowledgments* heading the second name should read Dr Wright.

Anaesthesia, 1991, Volume 46, page 333

The review on the book *Introduction to intensive care* was printed in error. The book has been withdrawn and we apologise for this inadvertent inclusion.

Anaesthesia, 1991, Volume 46, page 174–176

The alkalinisation of bupivacaine for intercostal nerve blockade

D. G. SWANN, P. J. ARMSTRONG, E. DOUGLAS, M. BROCKWAY AND G. M. R. BOWLER

The third sentence of the third paragraph in the Methods section of the above paper should have read:

Either 0.25 ml of normal saline (pH 4.1) or 0.25 ml 8.4% sodium bicarbonate (pH 6.9) were added to 10 ml of the bupivacaine solution; the percentage of uncharged drug is 0.1% and 7.1% respectively.

Contents: Anaesthesia, vol. 46, no. 8, August 1991

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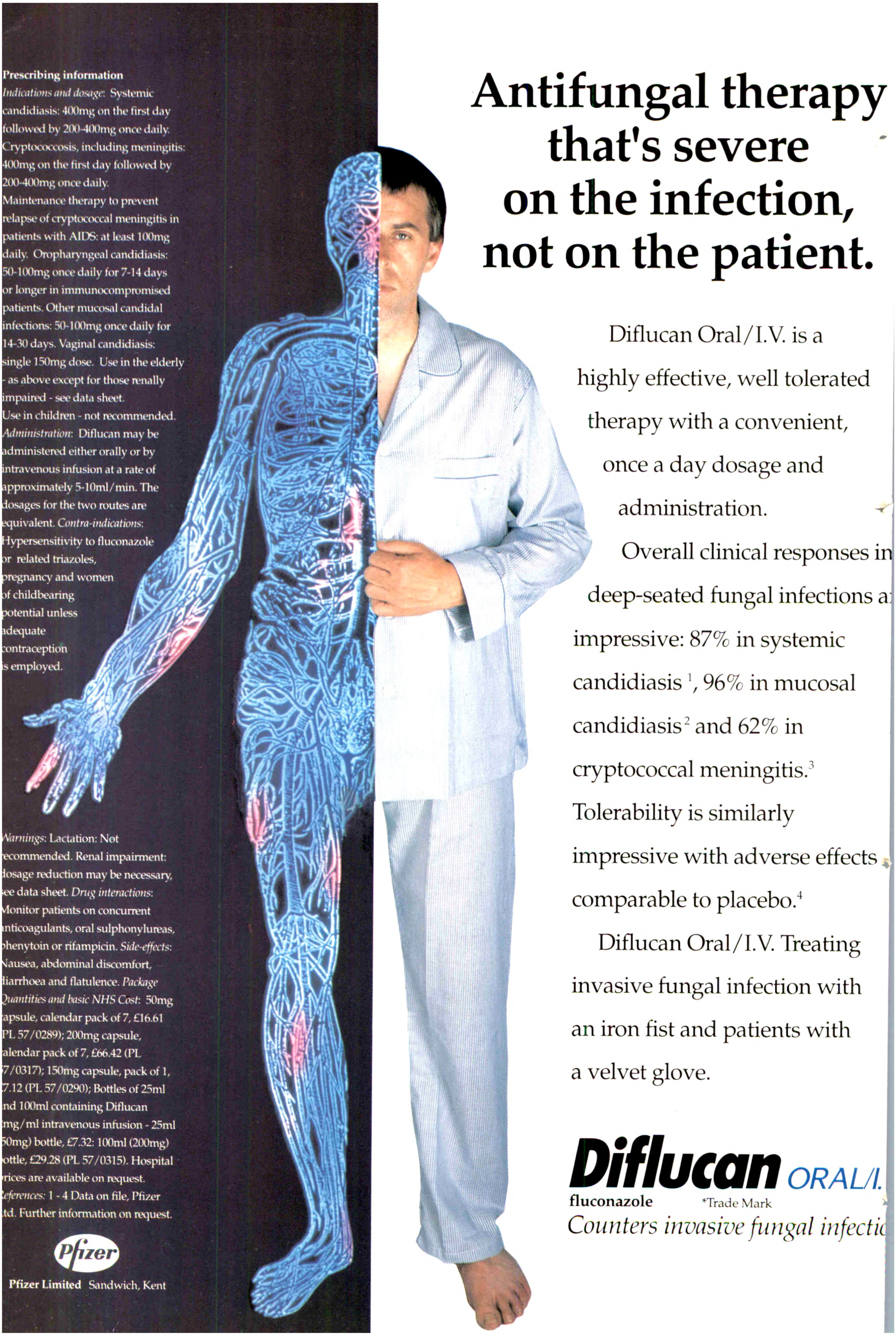
Prescribing information
Indications and dosage: Systemic candidiasis: 400mg on the first day followed by 200-400mg once daily. Cryptococcosis, including meningitis: 400mg on the first day followed by 200-400mg once daily.
Maintenance therapy to prevent relapse of cryptococcal meningitis in patients with AIDS: at least 100mg daily. Oropharyngeal candidiasis: 50-100mg once daily for 7-14 days or longer in immunocompromised patients. Other mucosal candidal infections: 50-100mg once daily for 14-30 days. Vaginal candidiasis: single 150mg dose. Use in the elderly - as above except for those renally impaired - see data sheet.
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Anaesthesia

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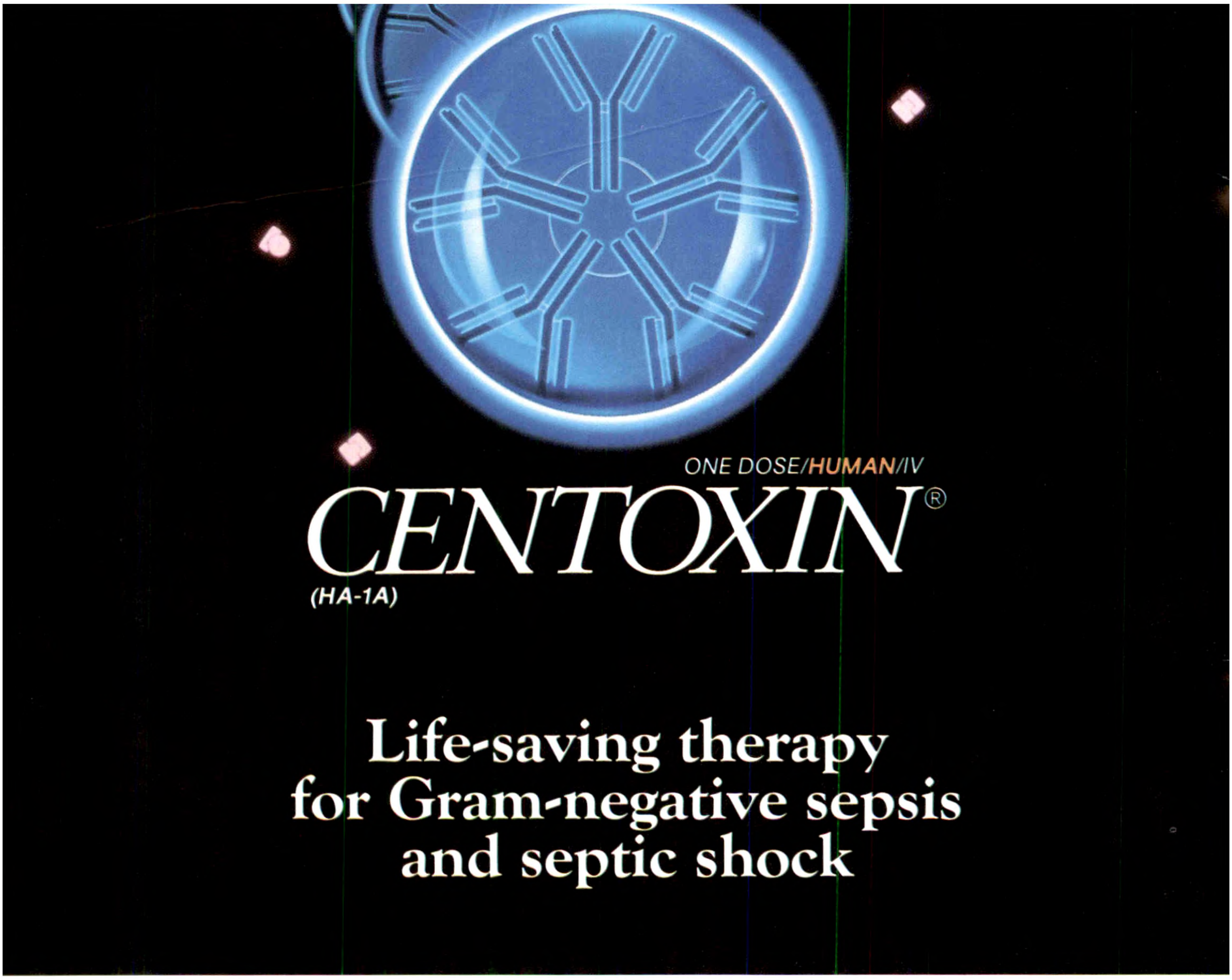

ABBREVIATED PRESCRIBING INFORMATION

PRESENTATION Centoxin is a solution for intravenous infusion after dilution with normal saline. Each vial contains: HA-1A 100 mg/20 ml

USES Centoxin is indicated for the treatment of patients with the sepsis syndrome and a presumptive diagnosis of Gram-negative bacteraemia, especially those with septic shock. Centoxin therapy should be given in hospital, along with the appropriate antibiotics and supportive therapy, as soon as Gram-negative sepsis is clinically suspected. Centoxin should be given once and is not intended for repeated use.

DOSAGE AND ADMINISTRATION The recommended dose of Centoxin is a single 100 mg intravenous infusion. Centoxin should be administered intravenously over a period of 15 to 30 minutes in a total volume of 70 mL after dilution with normal saline for injection. In patients studied to date, it has not been necessary to adjust the dosage for renal or hepatic function.

CONTRA-INDICATIONS, WARNINGS ETC. Contra-indications Centoxin should not be used in patients whose primary injury involves burns, since no studies have been done in those patients. Centoxin should not be used in patients with known hypersensitivity to murine proteins. Centoxin should not be used in patients with previous exposure to HA-1A. **Undesirable Effects** No serious or life-threatening adverse reactions attributable to Centoxin were reported among the more than 300 patients who received the product in clinical trials, including more than 45 patients who received 200 or 300 mg of HA-1A as a single dose. Transient flushing, localized urticaria and hypotension have been reported rarely (<1%) in patients receiving Centoxin. Human antibodies against Centoxin have not been detected. **Special Precautions** *In vitro* and *in vivo* mutagenicity studies have not demonstrated any mutagenic effect. Studies have not been performed to evaluate the carcinogenic potential or effects on fertility in male or female animals. The use of Centoxin in children has not been extensively studied. Centoxin has been administered to a small group of children (ages 10 months to 13 years), the majority of whom had fulminant meningococcaemia with shock and purpura. The dose administered was up to 6 mg/kg to a maximal dose of 100 mg. Centoxin was well tolerated by all patients. The efficacy of Centoxin in adults and children with meningococcal septicaemia has not been established and therefore the use of Centoxin in meningococcal septicaemia cannot be recommended. Centoxin contains a murine J chain, which suggests that anti-HA-1A

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Anaesthesia, 1991, Volume 46, pages 709–711

Editorial

Getting there

Earlier this year saw the publication of the 12th Triennial Report on Confidential Enquiries into Maternal Deaths,[1] representing the longest running series of continuous clinical audit in the world. Since its inception in the early 1950s, there has been a dramatic fall in maternal mortality, the number of deaths being approximately halved each decade, from 989 per million maternities in 1951 to 86 per million in 1982–84.

The pattern of maternal deaths is interesting. It remained relatively constant between 1847 and 1937 at about 4000 per million,[2] despite the introduction of significant advances which should have reduced it, such as the work of Semmelweis and Lister on antisepsis and asepsis. In the 1920s and 1930s a large proportion of these deaths were caused by excessive use of forceps delivery under chloroform anaesthesia administered by general practitioners. In 1930–32 there was a higher mortality rate among wives of men in professional and managerial occupations than among the wives of manual workers, whose deliveries tended to be supervised by midwives, rather than doctors.[2] The sudden reduction in death rate in 1937 was attributed to the introduction of sulphonamides, but undoubtedly other factors also played a part, such as improved blood transfusion, ergometrine, antenatal care, an increase in hospital confinement and especially better teaching resulting from the foundation of the (Royal) College of Obstetricians and Gynaecologists.

In the triennium 1985–87, eight mothers died as a direct result of receiving an anaesthetic. This represents a significant reduction from the previous report, when anaesthesia was the third commonest cause of death at 13.0%, to being equal last (4.1%) with ruptured uterus.

In order to look at anaesthetic death rates properly, it is necessary to relate them to the number of anaesthetics given, and this includes the use of epidural analgesia for pain relief. Exact figures, particularly for the latter, are not known, but there is no doubt that they are increasing. The abortion act did not exist during the first 18 years of the enquiries. There were 299 529 legal abortions in 1970–72, which increased to 475 330 in 1985–87; all required anaesthesia. The number of Caesarean sections increased from 103 310 in 1970–72 to 185 820 in 1982–84 (figures are not available from 1985 as the relevant body no longer exists following the purge on 'quangos'). To this must be added the fact that the present report, for the first time, covers all maternal deaths in the UK, previous reports being confined to England and Wales. This has been necessary because the number of deaths involved is now quite small and inclusion of Scotland and Northern Ireland (who previously conducted their own enquiries) will help to maintain the confidentiality that is so essential for the continuation of the enquiries. Although the number of direct deaths due to anaesthesia has fallen, there has been an increase in the number where anaesthesia might have contributed. However, it has been pointed out that this probably reflects the changing role of the anaesthetist, who is now much more closely involved in the management of seriously ill patients, such as those with massive haemorrhage or severe pre-eclamptic toxaemia.

The most important factor in the reduction in anaesthetic-related maternal mortality was the change in attitude to obstetric anaesthesia amongst anaesthetists in general in the mid and late 1960s. Previously, apart from a few enthusiasts, obstetric anaesthesia was regarded as little more than a nuisance. In reality, of course, it is one of the most challenging and rewarding branches of our specialty. No longer do we see statements such as that which concerned a Caesarean section under spinal anaesthesia '... initially satisfactory, but respiratory difficulties occurred before the operation was completed. By this time the anaesthetist was elsewhere and not immediately available.'[3] Even in the triennium 1967–69 comment was made that '.. 2 patients were found to be dead on transfer from the operating table to the trolley ...'[4] Anaesthetists now actively search for consultant posts with obstetric sessions. The College of Anaesthetists, prior to recognition of junior posts for training purposes, insists on proper equipment and facilities for obstetric anaesthesia, with a named consultant in charge. The basic principles of obstetric anaesthesia are widely taught on courses and manuscripts on the subject are amongst the most common submitted to anaesthetic journals. The Obstetric Anaesthetists Association is one of the most active of the specialist societies. It is these factors rather than any specific point that has led to the reduction in deaths due to obstetric anaesthesia.

Indeed, it is difficult to pick on any particular entity and relate it to a reduction in maternal mortality. The argument as to whether regional anaesthesia for Caesarean section is safer for the mother than general anaesthesia will never be settled, as a controlled trial is impossible. The increased use of epidural and spinal anaesthesia coincided with the increased interest in obstetric anaesthesia. The major problems of general anaesthesia, namely difficulty in tracheal intubation and inhalation of gastric contents, are swapped for those of cardiovascular depression and toxicity of local anaesthetics. The extensive sympathetic block produced by an epidural or spinal demands close monitoring of the cardiovascular system, particularly in patients with cardiac disease.[1] Fluid loading of the circulation to prevent hypotension is singularly ineffective.[5] This is not surprising as vasodilatation is the cause of the hypotension and vasoconstriction is the logical method of preventing and treating the reduction in arterial blood pressure.

Much has been written about the problems of inhalation of gastric contents and on methods to ensure that the pH of these contents in *all* labouring women be maintained above 2.5 But is this logical? There is no evidence that any of the mothers who died from 'acid aspiration' actually did so, because the pH of the inhaled material was not measured. As antacid prophylaxis has been routine in this country for some 25 years

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it would be reasonable to assume that the pH of the intragastric contents of most of the mothers would be well above 2.5. Thorburn and Moir[6] pointed out that treating all women in labour with some form of antacid therapy is not sensible, as each year a very large number of mothers will be receiving treatment in the hope of preventing a condition from which they are not at risk of suffering, since they are not going to receive a general anaesthetic. They gave cimetidine 200 mg intramuscularly immediately a decision was made to perform a Caesarean section and sodium citrate 30 ml just prior to general anaesthesia in 100 mothers who had not received antacid therapy in labour. No patient had an intragastric pH of less than 2.7 and only one less than 3.0. They pointed out that the regimen is simple and effective and treats only those at risk of acid aspiration. Perhaps we should be thinking more along these lines than treating so many mothers unnecessarily. It is noteworthy that an Australian survey (where anaesthetic practice is very similar to the UK) of all hospitals providing an obstetric service revealed that antacid prophylaxis was only used in 22.4% of the 379 hospitals (67%) that responded.[7] Cimetidine and ranitidine were rarely used. The above is not meant to imply that antacid prophylaxis should cease. Animal work by James *et al.*[8] has shown that the lower the pH of the inhaled materials, the smaller the volume needed to cause death. Other animal work has shown that nonacid aspiration is far from a benign process, especially when the inhaled material is particulate.[9] The only study in humans relating the pH of the aspirate to outcome showed that mortality was directly related to the degree of acidity.[10] However, the numbers were very small and the patients were already critically ill in an intensive care unit.

The reaction to the question of what is the critical volume of the aspirate to cause severe problems has certainly been illogical. The figure quoted is 0.4 ml/kg, which translates to about 25 ml in the average mother and relates to a statement in a paper referring to preliminary work in the Rhesus monkey.[11] Thus mothers at risk are defined as those having an intragastric volume greater than 25 ml and a pH of less than 2.5. It would appear that this figure is based on work performed on one monkey where 0.4 ml/kg of acid of pH 1.26 was instilled entirely into the right main bronchus; a similar volume of gastric juice buffered with THAM to pH 7.45 had already been instilled into the left lung.[12] More recent work in primates has shown that aspiration of 0.4 and 0.6 ml/kg at pH 1.0 only produced mild to moderate changes in the lungs.[13] Volumes of 0.8 and 1.0 ml/kg were associated with increasing pulmonary damage, 50% of the animals dying at the larger volume. This work would suggest that the critical volume in humans would be at least twice the commonly quoted figure. The words of Keats in the 8th TH Seldon Distinguished Lecture are pertinent:[14] 'One has to wonder why we behave in this way. Why is it we cannot wait for reasonable answers before going off half-cocked, full-steam-ahead to fight dragons and problems not known to exist?'

Failure and difficulties with tracheal intubation are now more common than gastric aspiration as a cause of death. This should not be. Scott has pointed out that patients do not die from failure to intubate the trachea, but from failure to stop trying to intubate the trachea.[15] After an absolute maximum of three attempts, in a mother paralysed with suxamethonium, the lungs must be ventilated via a face mask. Sellick[16] has shown that proper application of cricoid pressure will allow ventilation of the lungs with a face mask without inflation of the stomach. Anaesthetists have been reluctant to do this in patients with a potentially full stomach for fear of encouraging regurgitation. Such advice actually appeared in the fifth report. The exact procedure to be followed when tracheal intubation is abandoned will depend on the circumstances and the experience of the anaesthetist. A laryngeal mask airway may be extremely useful. Re-paralysing the mother after the suxamethonium has worn off is potentially very hazardous and should be avoided.

There are numerous methods described to diagnose the incorrect placement of a tracheal tube, but the essential piece of apparatus, which should be present wherever obstetric anaesthesia is administered, is a capnograph. This will inform in a couple of breaths whether the tube is in the trachea. A pulse oximeter has no place for this purpose, as the situation may be irretrievable before a pulse oximeter warns of incorrect tracheal tube placement. When this instrument alarms it basically means that something happened a few minutes earlier that the anaesthetist has missed.

Death due to problems with equipment and misuse of drugs has now virtually disappeared from the report. Care must, however, be taken to ensure adequate reversal of neuromuscular blocking drugs. It is not necessary to use long acting relaxants such as tubocurarine, pancuronium or alcuronium for Caesarean section. Use of a nerve stimulator is mandatory. It is also apparent that proper recovery facilities should be available for obstetric patients, the standard being the same as that provided in main operating theatres. A wise rule is to regard every patient who is restless postoperatively as hypoxic, until proved otherwise.

Obstetric anaesthetists in the UK provide a very high standard of care for their patients of which they can be justifiably proud. The maternal mortality reports provide documented evidence of such care. It is important that standards be maintained and this will not be easy in the new era into which we are moving. Managers will query large items of expenditure (and some all expenditure) and will use the time old argument 'Why didn't you want it before?' and 'if anaesthetic mortality is so low, is it really justifiable?' Anaesthetists must not compromise in their attempts to maintain a properly equipped and staffed obstetric anaesthetic service, unpopular though they will undoubtedly be. One mother dying as a result of an anaesthetic may represent only a very small percentage of the overall picture, but it is 100% for that patient and her family.

In a lecture on anaesthetic mortality, Keats[14] stated: 'I believe wishful thinking is the only basis for believing anaesthesia mortality today is less than it was 40 years ago.' As far as obstetric anaesthesia is concerned, the maternal mortality reports have produced documented evidence to refute this argument. It is perhaps too much to hope that a triennium will pass when there were no deaths due to anaesthesia, but perhaps we now have some evidence that we might be getting there.

M. Morgan

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Editorial notices

Manuscripts must be submitted in accordance with the internationally recognised *Uniform requirements for manuscripts submitted to biochemical journals* (*British Medical Journal* 1979: **1:** 432 5). Details will be found in the Notice to Contributors to *Anaesthesia* at the end of this issue.

Anaesthesia, 1991, Volume 46, pages 712–715

The first 24 hours after surgery

A study of complications after 2153 consecutive operations

M. GAMIL AND A. FANNING

Summary

The first 24 hours of the postoperative course of 2153 consecutive patients who had operations at the Nottingham Hospitals were studied in detail. Five per cent of patients had serious complications during this period; 15% of those having major operations, 1.8% having intermediate operations and 1.4% having minor operations. Thus, a significant number of patients were in an unstable condition for many hours after they were discharged from the main theatre recovery areas to the surgical wards. In 17 out of 23 patients who died and six out of six patients who suffered severe disability as a result of their surgery, the final outcome was a direct result of a sequence of events which began with an initial deterioration within 24 hours of surgery. We considered that, for at least 10 of these 29 patients, the outcome might have been different had more sophisticated postoperative facilities been available. In the light of this study we have identified the operations for which high dependency facilities are most likely to be required.

Key words

Recovery; complications.
Surgery; postoperative period.

As surgery becomes more complicated and the patients undergoing it are older and thus subject to more pre-existing disease, an increased incidence of life-threatening complications can be expected in the early postoperative period. The following quotation is taken from an editorial written after the publication of the *Confidential enquiry into perioperative deaths* (CEPOD):[1] 'If it is remembered that the common stated causes of death in surgical patients in the CEPOD study can all be classified as cardiorespiratory problems, the data may point to the need for much more intensive study of the postoperative period to determine how much of this is preventable with greater collaboration between the disciplines'.[2]

This study was undertaken to find the incidence of major problems occurring in the first 24 hours after surgery and to explore the possible relationship between such incidents and the eventual outcome of the patient. The second aim was to identify the patients most likely to benefit from high dependency facilities.

Method

An initial pilot study was undertaken which lasted 7 days and involved 330 consecutive operations. This gave us an indication of how long the main study would take, what data needed to be collected and the difficulties likely to be encountered.

The main study involved 2153 consecutive operations in all the major specialities (excluding neurosurgery and thoracic surgery) undertaken at the University and City Hospitals, Nottingham. The investigators were four anaesthetists, the authors and two others. Each day two people collected the data, between 0600 hours and midday. The operating lists from the previous day were obtained and any alterations noted. On the wards the nursing staff were questioned about any patient who had given cause for concern, and the nursing record of that patient examined. All patients who had had surgery in the preceding 24 hours were interviewed and asked about their well being and the adequacy of their pain relief. Observation, fluid and prescription charts were inspected. Table 1 shows the specific data recorded for each patient. If any of the documented complications occurred, the patient was followed up on subsequent days until the outcome became clear. The records of all cardiac arrest calls in the previous 24 hours were obtained from the telephone switchboard.

The study was continued until the target was reached. At the University Hospital over 1000 patients were collected in 16 days; at the City Hospital it took 22 days to collect the same number. Details of patients who died within 30 days

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Table 1. Patient data and postoperative complications recorded.

Patient data
Name
Age
Ward
Operation
ASA grade (if complications recorded)

Complications
Cardiac arrest
Admission to intensive care unit
Myocardial infarction
Angina
Arrhythmias
Cerebrovascular accident
Transient ischaemic attack
Confusion
Oliguria (<0.25 ml/kg/hour over 2 hours)
Respiratory complications
Hypotension (a systolic blood pressure of <100 mmHg if it was also > 30 mmHg below pre-operative recording. Blood and colloid transfusion was noted)

of surgery were obtained from the Patient Information Services Division.

Results

The data were collected on 2153 patients. Table 2 shows the classification of surgery into major, intermediate and minor. Eight hundred and one (37%) had minor surgery, 784 (36%) intermediate surgery and 568 (26%) major surgery. Table 3 shows the contribution of each specialty to the total surgical workload. Table 4 details the post-operative problems which were documented and their outcome. Table 5 relates the complication rate to age.

Table 2. Classification of procedures.

Major
Arterial surgery
Abdominal surgery (general and gynaecological)
Oesophageal surgery
Open urological procedures
Transurethral prostate and tumour resections
Vaginal hysterectomy
Caesarean section
Joint replacement
Fractured femur
Spinal surgery
Multiple injuries
Complex oral, ear, nose and throat surgery
Burns surgery
All equivalent operations

Intermediate
Hernia repair
Varicose veins
Ophthalmic surgery
Laparoscopy
Tonsillectomy
Dental surgery
Other equivalent operations

Minor
Dilatation and curettage
Cystoscopy
Minor body surface operations
Orthopaedic manipulations
Other equivalent operations

Table 3. Number of operations classified by individual specialty. The percentage of major operations, emergency surgery and emergencies classified as major cases, is shown for each specialty.

Specialty	Total *n*	Major (%)	Emergency (%)	% of major as emergencies
General surgery	543	26.3	22.3	30.1
Obstetric/ gynaecology	732	20.7	29.0	25.0
Orthopaedic	241	41.5	52.3	79.0
Urology	250	38.8	3.2	4.1
Plastic/burns	97	46.4	14.4	31.1
Ear, nose and throat	158	9.5	1.9	0.0
Oral surgery	70	22.9	5.7	26.7
Ophthalmic/GA	62	0.0	9.7	0.0
Totals	2153	26.4	22.9	32.0

GA: general anaesthesia.

One hundred and nine patients (5%) had major complications and were in an unstable condition, (by this we mean that serious and potentially life-threatening events were recorded) for some hours after discharge from the theatre recovery area. There were 23 deaths and six patients were subsequently discharged with serious disabilities; this term is used to indicate a serious decrease in cardiac, respiratory

Table 4. Causes of postoperative problems and the outcome (numbers of patients).

	Major surgery (*n*)	Minor or intermediate surgery (*n*)	Deaths (*n*)	Serious disability (*n*)
ITU admission	28	1	5	—
Cardiac arrest call	4	1	4	—
Cerebrovascular accident (CVA)	1	—	—	1
Transient CVA	2	—	—	2
Myocardial infarction	2	—	1	—
Angina	—	1	—	—
Confusion	6	2	2	—
Hypotension	33	15	3	2
Hypertension	1	—	—	—
Oliguria	2	—	2	—
Opioid-induced respiratory depression	1	1	—	—
Other respiratory complications	3	1	—	1
Urinary retention	1	—	—	—
Hypoglycaemia	—	2	—	—
'Collapse' after buprenorphine	—	1	—	—
Totals	84	25	17	6

Table 5. Major surgery: postoperative complications related to age.

Age range (years)	<17	17–44	45–60	61–70	71–80	81+
Incidence of complications after major surgery (%)	2.3	7.6	11.6	19.6	28.7	27.6

Table 6. Type of operation and percentage with postoperative complications; deaths and potentially avoidable deaths.

Operation	Total (*n*)	% with complications	Deaths (*n*)	Avoidable deaths (*n*)
Emergency laparotomy	45	60	8	1
Fractured femur	20	40	4	1
Multiple injury	5	100	0	0
Aortic aneurysm, elective	5	100	1	0
Femoropopliteal bypass	3	100	0	0
Transurethral resection of tumour	9	44	1	1
Elective 'open' urology	21	33	1	1
Transurethral resection of prostate	63	11	0	0
Elective laparotomy	37	24	5	0
Abdominal hysterectomy	47	8.5	0	0
Mastectomy	20	10	0	0
Hip replacement	4	25	0	0
Hernia repair (number not known)	—	—	1	0

or neurological reserve, to an extent that a patient who was ambulant at home before admission left hospital wheelchair dependent, or in need of nursing care. The mortality rate was 0.24% at 24 hours, 0.3% at 48 hours and 0.8% at 30 days.

Minor and intermediate surgery

Twenty-five patients out of the 109 were in these two categories. Eleven had had minor surgery, and 14 intermediate surgery; respectively 1.4% and 1.8% of minor and intermediate surgical cases. Cardiac arrest calls were initiated for two of these patients; one had opiate-induced respiratory depression, the second was an ASA 4 patient who subsequently died at home. Fifteen patients in this group developed hypotension within 3 hours of surgery, and in 13 this was unexplained. There were no common anaesthetic or surgical factors. All patients experienced dizziness and this symptom often outlasted the period of hypotension. Resolution was from one to 20 hours after operation; the average was 4 hours. Twenty-four of the 25 patients with complications completely recovered.

Major surgery

Eighty-four patients who had major surgery were unstable in the first 24 hours after operation. These patients represented 15% of the major operations. Sixteen of them died subsequently, while a further six had severe residual disability. Thus 23 out of 29 patients in whom the outcome was death or severe disability began their deterioration within 24 hours of surgery. We considered that the outcome might have been better in 10 patients, (four of those who died, and all six of those with permanent disability), had their initial deterioration been prevented or managed more aggressively.

Table 6 shows the relationship between serious complications in the first 24 hours and the type of operation performed. It can be seen that patients with certain types of surgery are at a particularly high risk of instability in the early postoperative period. Elective repair of aortic aneurysm, femoropopliteal bypass, multiple trauma, emergency laparotomy, transurethral resection of bladder tumour, fractured femur and open urological operations were associated with the highest incidence of early postoperative instability. These seven groups also accounted for

Table 7. Incidence of postoperative problems in elective and emergency major procedures for each surgical specialty.

Surgical specialty	Elective major (*n*)	Incidence of problems %	Emergency major (*n*)	Incidence of problems %
General surgery	100	19	43	53.5
Obstetrics/ gynaecology	114	3.5	38	10.5
Orthopaedic surgery	21	4.7	79	16.5
Urology	93	17.2	4	100
Plastic surgery	31	0	14	0
Ear, nose and throat	15	6.6	0	0
Oral surgery	12	0	4	0

the majority of surgically-related deaths and poor outcomes. The incidence of problems in the different surgical specialties for elective and emergency surgery are detailed in Table 7.

Discussion

In this study, the incidence of serious complications in the first 24 hours after operation was 5 per 100 theatre cases. Our first aim was to investigate the relationship between problems in the early postoperative period and subsequent poor outcome. In this study, 21% of patients who had problems in the first 24 hours subsequently died or suffered severe disability and 80% of those in whom the final outcome was bad, started to deteriorate within 24 hours of surgery.

Our second aim was to identify the types of surgery following which patients would most benefit from provision of 24-hour recovery or high dependency facilities. A significant percentage of patients with major surgery remained in an unstable condition for 24 hours after operation and the seven categories named above were associated with a particularly high incidence of complications.

It was clear from the study that there was an association between early postoperative deterioration and either death or serious morbidity. In addition, we found that death and serious morbidity (inevitable or preventable), were distributed evenly across the surgical specialties. However, certain operations were associated with a particularly high incidence of early postoperative complications. In the light of this study we suggest that patients who have certain operations would benefit from additional nursing and medical resources in the early postoperative period. The surgical procedures referred to include complex major surgery including vascular surgery and multiple injury; emergency laparotomy in patients with benign conditions or with malignant disease in whom there is a reasonable prognosis; fractured neck of femur; all major urological procedures.

We consider that, had high dependency facilities been available for these groups of patients, at least 17% of the surgical deaths and all of the permanent disabilities might have been prevented.

Previous studies of postoperative morbidity and mortality have varied greatly in their methods of collection and presentation of data.[3-8] The Vancouver study[5] and the U.S. Naval Hospitals'[6] study are mortality reports only. The multiregional French study[4] is primarily concerned with anaesthesia-related deaths and serious outcome. The Winnipeg Health Sciences Centre reports encompass, on average, 50% of their cases and document all anaesthesia-related complications, minor and major.[7,8] Thus comparisons between these papers and our own study was not possible, although there was some suggestion that we may have observed a higher incidence of opiate-induced respiratory depression. Our 24-hour death rate (0.24%) is comparable to that reported by Vacanti *et al.* (0.39%).[6] Our death rate at 48 hours (0.3%) is of similar magnitude to that in the Vancouver study (0.22%)[5] and our 30-day mortality rate of 0.8% compares with that of the British CEPOD study (0.8–1.0%).[1] We have found a similar age-related pattern of problems to other studies. Although the incidence of certain complications, such as haemorrhage, are not age-related, the older patient is less able to cope with the associated physiological disturbances.

During this study, although we observed some instances of substandard care on the postoperative wards, in the majority of cases the incidents which occurred were due to misadventure (e.g. silent aspiration of stomach contents). Such misadventures must be anticipated and provided for in the first 24 hours after operation. In the case of a sick patient recovering from major surgery, this early period might be considered to be a 'physiological obstacle course'. It is incorrect to assume that such events are simply the result of bad anaesthetic or surgical practice, or even that they are all preventable. Many complications are inevitable, but in order for resulting damage to be minimised, close monitoring is essential and rapid, skilled treatment of complications is required. This can only be provided in a 24-hour recovery or high dependency area, staffed by nurses and clinicians familiar with the management of postoperative problems. It has been suggested in a recent editorial that clinical researchers in anaesthesia should address themselves to the important hazards of the first postoperative week.[9] The results of this study suggest that, after certain categories of surgery, the first 24 hours is a particularly critical period. Special postoperative facilities should be available for these patients.

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Plasma etomidate levels in mother and fetus

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Summary

The most commonly used induction agent in anaesthesia for Caesarean section is still thiopentone. The increasing incidence of Caesarean section for delivery of premature babies from a hostile environment may call in question the assumption that the dose of thiopentone received by the neonate will not cause depression in the hours following birth. Previous studies on thiopentone for Caesarean section have shown inconsistency in umbilical vein/maternal vein ratios. We have studied plasma etomidate levels in maternal and umbilical blood at the time of delivery to see whether equilibrium occurs with this agent. We were able to demonstrate an umbilical/maternal vein etomidate ratio of 0.5 (SD 0.18), with no relation to time in the range encountered. Also, the uterine artery/uterine vein etomidate ratio was 0.86 (SD 0.33), suggesting that etomidate uptake into the fetus is effectively complete. Further, in all cases the neonatal plasma etomidate levels were less than half those measured at recovery of consciousness in adults in other studies, despite a larger induction dose than is usually used.

Key words

Anaesthetics, intravenous; etomidate.
Placental transfer; etomidate, fetal/maternal ratio.

Studies with thiopentone[1–4] have shown great variation in blood levels in maternal and fetal circulations at the time of delivery. Some studies[1,2,4] have shown that fetal levels are equivalent to maternal levels, whilst others[3,5] have demonstrated a gradient. One of the reasons for this may be the difference in the induction–delivery (ID) intervals; those studies showing parity tending to be associated with longer ID times. Etomidate is a carboxylated imidazole derivative first introduced into clinical practice in 1973. It has been used satisfactorily in obstetric anaesthesia since 1979.[6,7] The rapid elimination and short recovery time following its use[8,9] suggested that etomidate might be a suitable drug for induction of anaesthesia for Caesarean section. Although thiopentone has proved to be safe for both mother and fetus during use for Caesarean section, a previous study[6] suggested that there might be a slight advantage from the use of etomidate. The present study was undertaken to determine the relative plasma etomidate levels in maternal and fetal blood at the time of delivery.

Method

Approval for the study was obtained from the district ethics committee, and informed consent was obtained from all participants in the study. Women of ASA grade 1 undergoing elective Caesarean section for a singleton pregnancy, with no evidence of placental dysfunction, pre-eclampsia or overt supine hypotension, were entered into the study. Patients were given 30 ml 0.3 M sodium citrate before the start of anaesthesia. They then lay on a trolley with 15° left lateral tilt. A 16-gauge intravenous cannula was inserted under local anaesthesia and the patient was pre-oxygenated for 3 minutes. Anaesthesia was induced using a rapid sequence induction technique with cricoid pressure. Each woman received etomidate 0.4 mg/kg given intravenously over 30 seconds followed by suxamethonium 1.0 mg/kg. Anaesthesia was maintained with 50% nitrous oxide in oxygen and 2% halothane for one minute and then 0.5% until delivery. Muscle relaxation was maintained with an initial dose of atracurium 0.5 mg/kg.

A maternal venous sample was taken at the time of delivery of the fetus from the contralateral arm to that used for induction. Umbilical venous and arterial samples were also obtained from a section of umbilical cord, cross-clamped at delivery. The samples were immediately centrifuged and the plasma separated and frozen for later analysis. The samples were divided into seven batches and were analysed using high pressure liquid chromatography by a modification of the method of Ellis and Beck.[10] The preci-

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Table 1. Demographic data and mean maternal and umbilical plasma etomidate concentrations at delivery.

	Number	Mean	SD
Age; years	20	27.6	8.8
Weight; kg	20	68.8	11.3
Plasma etomidate concentration; μg/litre			
Maternal	20	198.8	73.9
UV	20	92.7	31.7
UA	7*	62.9	33.3

UV, umbilical venous; UA, umbilical arterial.
* Insufficient blood available in 13 cases.

sion of the method was calculated at the level of 100 μg/litre. The between-batch coefficient of variation was 10.15%. The limit of detection was 20 μg/litre.

Statistical analysis was carried out using the Student's *t*-test and regression analysis.

Results

A total of 20 women (four primagravida, 16 multigravida) were recruited into the study. The range of induction–delivery (ID) times was 9–22 minutes (mean 15.2, SD 3.8). This reflects the fact that many of these were repeat operations with a variable degree of difficulty for the operator due to scar tissue. The uterine incision to delivery time was less than 90 seconds in all cases. In 13 cases we were unable to obtain sufficient umbilical arterial blood for analysis.

There was a significant difference between the maternal and umbilical venous etomidate levels ($p < 0.001$). There was no significant difference between the values for umbilical venous and umbilical arterial etomidate levels ($p < 0.62$). Table 1 summarises the results. The ratios of the umbilical venous/maternal plasma etomidate levels (UV/MV) at delivery and umbilical arterial to umbilical venous plasma etomidate levels (UA/UV), in those cases where it was possible to obtain both, were calculated and the results shown in Figure 1. There was no relationship between ID time and either UV/MV or UA/UV ratios.

Discussion

The use of Caesarean section for delivery is increasing. There are many reasons for this, but two of the most important are: earlier antenatal recognition of those babies at risk from maternal disease (e.g. hypertension, pre-eclampsia) and those at risk from placental dysfunction. It is therefore important that the additional burden of depressant drugs should be minimised during operative delivery.

However, reports of maternal awareness during Caesarean section led us to increase the induction dose of etomidate from the recommended 0.3 mg/kg to 0.4 mg/kg and to use 2% halothane for the first minute postinduction in order to prevent awareness. There was no incidence of awareness or dreaming using this technique.

This study demonstrates a UV/MV ratio of 0.5 (range 0.08–0.88 SD 0.175). This was constant for the range of ID times in the study, implying that fetal redistribution was as rapid as that in the maternal circulation over the 9–22 minutes. Further, the UA/UV ratio of 0.864 (range 0.38–1.28 SD 0.329) suggests that uptake, redistribution

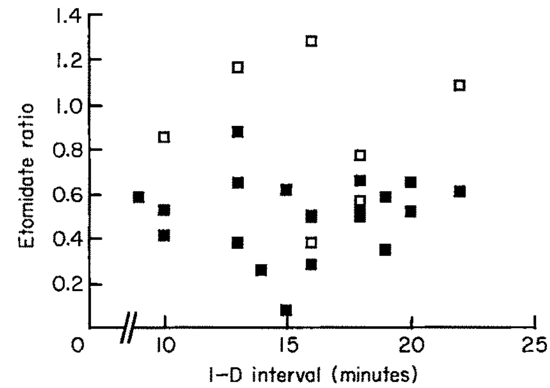

Fig. 1. UA/UV (□) and UV/MV (■) ratios with respect to time.

and/or metabolism was still taking place during the time course of this study, although the process was almost complete.

The measurement of fetal uptake of drugs is difficult both for ethical and methodological reasons. Despite the inadequacies of the technique, the sampling of umbilical cord blood at delivery is the only means available to study drug transfer in human neonates. Some of the factors that affect fetal drug levels are molecular weight, lipid solubility and degree of ionization. Etomidate is a small molecule, is fairly lipid soluble and is a weak base with a pKa of 4.2. It should therefore cross the placenta readily.

Differences in maternal and fetal levels of drug may be a reflection of binding to plasma proteins. Etomidate is 80% protein bound in adults. There are no data on its binding in neonates, but the albumin/globulin ratio in neonates is not very different from that in adults (umbilical cord blood albumin levels being 27–49 g/litre as opposed to 38–48 g/litre in the adult, and total protein being respectively 51–68 g/litre and 50–80 g/litre). Thus, the wide and constant differences in our series could not be the result of this factor alone.

In all cases Apgar scores were satisfactory (greater than or equal to 7 at 1 minute and 9/10 at 5 minutes). Further, etomidate levels were less than half the levels reported in adults at full recovery from etomidate anaesthesia,[11,12] despite increasing the induction dose by 30%, as explained above.

In conclusion, etomidate gives UV/MV ratios less than or equivalent to those obtained for thiopentone. It has been demonstrated in this and other studies[10] to give satisfactory conditions for induction of anaesthesia in elective Caesarean section. Although further study is needed, etomidate may well have a place in those situations in which the use of thiopentone might be relatively contra-indicated (e.g. ante-partum haemorrhage, fetal distress and maternal atopic disease).

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Intra-arterial blood sampling for clotting studies

Effects of heparin contamination

J. K. L. LEW, R. HUTCHINSON AND E. S. LIN

Summary

Prothrombin time and activated partial thromboplastin time were measured in two groups of 30 patients each. Blood sampled from an arterial line after various discard volumes and from a central venous line were compared with direct venipuncture control samples. The arterial line flushing solution contained 1 unit of heparin per ml in group 1 and 2 units per ml in group 2. Our results confirmed that clotting studies carried out on blood samples from an arterial line or central venous line correlate well with those obtained from a venipuncture sample. The only exception was activated partial thromboplastin time in group 2 patients when the discard volume from the arterial line is only 2.5 ml above the deadspace volume of the connecting line. At least 5 ml of discard volume must be withdrawn before sampling, to obtain reliable results.

Key words

Blood; coagulation, heparin.

In the Intensive Care Unit (ICU), blood is often taken from arterial lines for laboratory investigations. These lines are usually kept patent by a device which flushes a continuous infusion, 3–6 ml per hour, of a dilute saline solution containing one or two units of heparin per ml. Blood samples are often taken from these lines for clotting studies. However, there is concern about possible contamination with heparin from the flushing solution.[1]

This study was designed to assess the effect of heparin in the arterial line flushing solution on clotting studies. We looked at how the results were affected when different discard volumes were taken from the line and when two different heparin concentrations were used in the flushing solution. We also sought to discover whether central venous samples gave reliable clotting results.

Methods

The study was approved by the Chinese University of Hong Kong Ethics Committee.

Sixty patients admitted to our Intensive Care Unit were randomly selected, and included those with both normal and abnormal clotting. Those who were receiving heparin therapy were excluded; each patient was studied once only. All patients had a radial arterial line (Abbocath 20G) and an internal jugular central line (Abbocath 16G). In the first group of 30 patients (group 1), the arterial line flushing solution was prepared by adding 500 units of heparin to 500 ml of normal saline (1 unit per ml). For the rest of the patients (group 2), 1000 units were added to 500 ml of normal saline (two units per ml). The in-line flush device used (Model TA4004 Critiflow, Spectramed Inc., California) provided an infusion rate of 2–4 ml per hour. The deadspace from the arterial cannula to the sampling port was measured and found to be 0.6 ml.

A 2.5-ml blood specimen was sampled from the arterial line after withdrawal of discard volumes of deadspace plus 2.5, deadspace plus 5 and deadspace plus 10 ml. The arterial line was flushed after each sampling until the connecting tubing was clear of blood. A discard volume of 5 ml of blood was drawn from the central venous pressure (CVP) line followed by a 2.5 ml specimen. A further 2.5 ml of blood was obtained by venipuncture. All the 'discard volumes' were returned to the patient via a peripheral venous line. Each test sample was immediately placed in a blood specimen tube containing 2.5 ml of sodium citrate and mixed thoroughly. Prothrombin time (PT) and activated partial thromboplastin time (APTT) were measured, using an automated instrument (Cobas Fibro – F. Hoffman/La Roche and Co, Basle, Switzerland). The reagent used for the measurement of PT was Thromborel S (Behring, Marburg, W. Germany) and for APTT, Automated APTT (Organon Teknika Corporation, Durham, NC, USA). The quality control figures for our laboratory are shown in Table 1.

The data collected were subjected to statistical analysis using the Student's *t*-test and regression analysis.

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Table 1. Quality control figures for PT and APTT (derived from 100 tests on the same control sample performed over a 30-day period).

	PT (seconds)	APTT (seconds)
Normal range	12–14	25–40
Mean	12.36	33.34
SD	0.49	1.43
Coefficient of variation	3.97	4.29

Results

Three patients had to be withdrawn from the study and replaced because of incomplete data.

The PT and APTT results of the various samples obtained from the arterial and the CVP lines were compared with those drawn by venipuncture. In the group 1 patients (Table 2), there was a significant statistical difference only in the PT for the deadspace plus 5 ml and the CVP samples ($p < 0.05$). There was no difference between the samples for APTT. In the group 2 patients, there was no difference between the mean PT of all the groups when compared to that of the venipuncture group. There was a statistically significant difference between the mean APTTs of the deadspace plus 2.5 ml samples and the venipuncture samples ($p < 0.05$).

Table 3 shows that all the samples in the group 1 patients correlated well with those drawn by venipuncture ($p < 0.001$). In the group 2 patients, there is a good correlation when the PT results from the nonvenipuncture groups were compared with the venipuncture group. The APTT results were similar apart from the deadspace plus 2.5 ml group, which produced a poor correlation when compared with those for the venipuncture, with a correlation coefficient of 0.81 and a regression slope of 0.73.

Discussion

Blood sampling from arterial lines for laboratory investigations is common practice in the ICU because of its convenience and minimal interference with the patient. The validity of using such samples for clotting studies has been questioned[1] in view of possible contamination with heparin from the flushing solution. If abnormal results are obtained, the tendency is for the physician to blame it on contamination and repeat the tests. This is not only time consuming and expensive but more importantly can delay prompt treatment in patients with actual clotting defects.

Bark[2] in 1970 reported abnormal coagulation in blood samples drawn from a central venous catheter flushed with heparin to maintain patency. Merenstein[3] showed that blood passing through umbilical artery catheters flushed with heparin had a prolonged APTT unless 4 ml of blood was withdrawn before sampling.

Since then, numerous studies[4–7] have shown that reliable coagulation screens could be obtained from arterial lines provided certain conditions were satisfied. However, some of these studies had limitations such as the use of small numbers of subjects, lack of mention of deadspace volume of the arterial line, complicated placement of stopcocks and fixed discard volumes. Reinhardt *et al.*[7] studied the effects

Table 2. Mean (SD) values for PT and APTT in seconds for group 1 (heparin 1 unit/ml) and group 2 (heparin 2 units/ml). Statistical significance figures were obtained using Student's paired *t*-test with venipuncture sample as control.

	Group 1				Group 2			
	PT		APTT		PT		APTT	
VS	14.7 (2.8)		39.6 (7.6)		14.5 (2.2)		39.6 (6.2)	
Deadspace + 2.5	14.8 (2.9)	NS	40.7 (7.2)	NS	14.5 (2.3)	NS	41.2 (6.8)	$p < 0.05$
Deadspace + 5	14.9 (3.0)	$p < 0.05$	40.4 (6.9)	NS	14.6 (2.4)	NS	39.7 (5.9)	NS
Deadspace + 10	14.8 (3.0)	NS	39.8 (7.7)	NS	14.6 (2.3)	NS	39.3 (6.3)	NS
CVP	14.9 (2.9)	$p < 0.05$	40.0 (6.4)	NS	14.7 (2.3)	NS	39.9 (5.8)	NS

VS, venipuncture sample; CVP, central venous pressure; NS, not significant.

Table 3. Regression analysis: comparison with venipuncture group as control.

		Group 1		Group 2	
		C	RS	C	RS
PT	Deadspace + 2.5	0.98	0.93	0.98	0.96
	Deadspace + 5	0.99	0.92	0.98	0.91
	Deadspace + 10	0.98	0.91	0.98	0.95
	CVP	0.98	0.94	0.98	0.95
APTT	Deadspace + 2.5	0.91	0.91	0.81	0.73
	Deadspace + 5	0.93	1.01	0.93	0.98
	Deadspace + 10	0.93	0.92	0.91	0.90
	CVP	0.89	1.05	0.94	1.00

C, correlation coefficient; RS, regression slope.

of different discard volumes and heparin concentration in the flushing solution. There was no significant difference in test results between heparin concentrations of 1, 2 or 4 units per ml. They found that a minimum discard volume equal to five times the deadspace from the catheter tip to the sampling port is required if accurate and reliable coagulation studies are to be obtained. However, the use of the canine experimental model and the small number of subjects imposed some limitations on that study.

Our study is along similar lines to that of Reinhardt *et al.*[7] but we used human subjects in the clinical setting of an ICU. We also included blood samples from a central line. In patients who had 1 unit per ml of heparin flush solution (group 1), accurate results were obtained for PT and APTT for all the samples. Although the deadspace plus 5 ml and the CVP samples showed a statistically significant difference when mean PT values were compared with those from the venipuncture samples, these were well within the laboratory error margins and were not clinically significant. Regression analysis showed very good correlation between all the sampling methods compared to venipuncture. In patients who had a flushing solution of 2 units per ml of heparinised saline, there was no significant difference in PT when the samples were compared with the venipuncture control. There was, however, a significant difference from control for APTT when only 2.5 ml plus deadspace was drawn. This was confirmed by regression analysis which showed poor correlation ($r = 0.807$ and regression 0.73) when the deadspace plus 2.5 ml samples were compared with the venipuncture control samples.

In conclusion, we have found that arterial sampling is reliable for clotting studies. If the arterial line flushing solution contains more than 1 unit of heparin per ml, at least 5 ml of discard volume should be drawn to obtain good correlation with a venipuncture sample. Blood could also be sampled from a CVP line for clotting studies provided care is taken to avoid the introduction of infection.

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Observations on deliberate dural puncture with a Tuohy needle: depth measurements

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Summary

Observations were made during the use of a Tuohy needle to perform deliberate dural puncture for the insertion of lumbar drains to improve operating conditions for intracranial aneurysm surgery. The most striking finding was the distance from identification of the epidural space to penetration of the dura. We postulate that this was because of tenting of the dura by the blunt Tuohy needle. This was facilitated by the absence of a negative epidural space pressure because an open system was used, which allowed time for pressure equilibration. This minimised the reactive forces across the dura. Aspiration and rotation of the Tuohy needle revealed dural puncture in some cases.

Key words

Equipment; Tuohy needle.
Complications; dural puncture.

Lumbar cerebrospinal fluid (CSF) drainage is often helpful in reducing intracranial volume during intracranial aneurysm surgery, improving surgical exposure. At our institution the surgeon often requests that a catheter be introduced into the lumbar subarachnoid space to withdraw CSF intra-operatively. The insertion of these drains has been in the domain of the anaesthetist. Deliberate dural puncture is performed with a Tuohy needle and an 18-gauge epidural catheter is threaded into the epidural space. Contrary to expectations, deliberate dural puncture with a Tuohy needle can be surprisingly difficult, as can threading an epidural catheter into the subarachnoid space. This paper and the ensuing one describes some of our observations whilst performing this procedure.

Methods

Patients requiring lumbar drains who presented to one of the authors (T.E.H.) during the period March 1987 to January 1989 were included in the study. Dural puncture was performed in the left lateral position with the patient under general anaesthesia after the usual monitors had been placed. A disposable Tuohy needle (Portex) was used in some cases; in others a re-usable Tuohy needle was used. The L_{2-3} or L_{3-4} interspaces were used in all cases, together with a midline approach. The Tuohy needle was placed in the interspinous ligament and the epidural space was identified using loss of resistance to air. The skin-to-epidural space distance was noted. With the trocar removed, the needle was slowly advanced and dural puncture sought, as shown by free flow of CSF. If no CSF was seen after advancing the needle 1 cm, the needle was aspirated. If then there was no CSF flow, the needle was rotated through 360°. The needle was aspirated again if there was still no flow and if this was unproductive the needle was slowly advanced a further 1 cm and the previous sequence repeated. If still no CSF was obtained the needle was slowly advanced further. The distance from identification of the epidural space to dural puncture was noted. When CSF was obtained the rate of flow was classified as 'slow'—CSF dripped out of the Tuohy needle or 'fast'—continuous flow of CSF. Cannulation of the subarachnoid space was attempted with a Portex 18-gauge epidural catheter. In the event of failure with a Portex catheter, cannulation was attempted with a Racz catheter.

Results

A total of 31 patients were included in the study, 15 male (aged 17 to 74 years) and 16 female (aged 30 to 72 years). One male patient required lumbar drains for two separate procedures 6 months apart and was studied twice.

Figure 1 shows the frequency distribution of the distance from skin to the epidural space. Figure 2 shows the inci-

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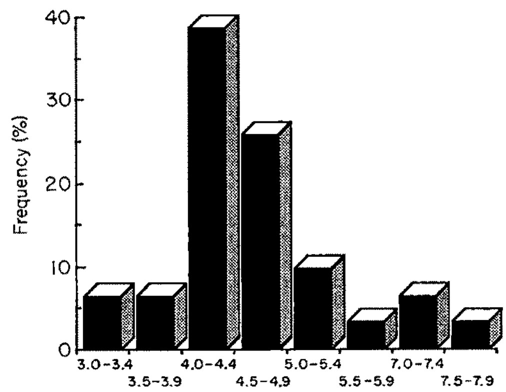

Fig. 1. The frequency distribution of the distance from the skin to the epidural space.

dence of dural puncture (ordinate) plotted against the distance from entry into the epidural space to dural puncture (abscissa). The abscissa displays this distance in centimetres with three extra points at the 1 and 2 cm marks to show the incidence of dural puncture during the 'aspiration, rotation, aspiration' sequence. All other points record spontaneous dural puncture.

There were no discernible differences between the two Tuohy needles used in the incidence of spontaneous or 'assisted' dural puncture. The incidence of slow CSF flow was not related to the depth at which dural puncture occurred (this occurred in eight cases). Dural puncture was unsuccessful in two patients in both of whom there was free flow of venous blood from the Tuohy needle. This was believed to be because of failure to remain in the midline and consequent puncture of the epidural venous plexus.

Subarachnoid space catheterisation was successful in 26 patients with the Portex catheter (89.7% of cases). All three patients in whom it was impossible to thread a Portex catheter were successfully catheterised with a Racz catheter (10.3% of cases).

Discussion

The increasing use of lumbar CSF drainage at our neurosurgical unit and the transfer of responsibility of the insertion of these drains from surgeon to anaesthetist in recent years has allowed us to observe the performance of Tuohy needles during dural puncture, an event that is more

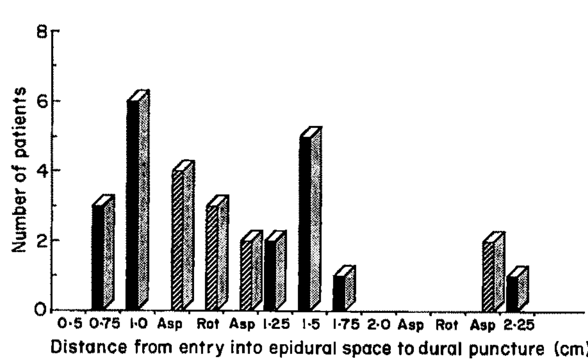

Fig. 2. The incidence of dural puncture plotted against the distance from identification of the epidural space to dural puncture. The hatched bars indicate when dural puncture was assisted by the 'aspiration (Asp), rotation (Rot), aspiration (Asp)' sequence. ▨, assisted dural puncture; ■, spontaneous dural puncture.

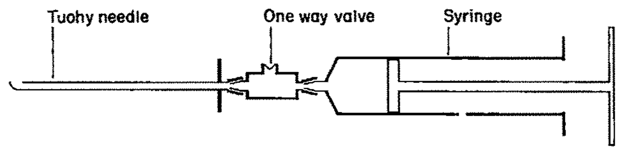

Fig. 3. This demonstrates the one-way valve in position between the loss-of-resistance device and the Tuohy needle.

normally rated as a complication of epidural anaesthesia. Since the original description of the use of the Tuohy needle for continuous spinal anaesthesia,[1] the needle has been used almost exclusively for epidural rather than subarachnoid catheter placement.[2] We were surprised at the distance from location of the epidural space to dural puncture in these patients, since reference texts quote smaller distances[3] and most anaesthetists have either first or second hand experience of the ease of inadvertent dural puncture with this needle. To assess the validity of our measuring technique we compared the skin-to-epidural space distances with previously published work and found them to be broadly comparable.[4] The unexpectedly large distance from identification of the epidural space to dural puncture may be because of dimpling of the dura with a relatively blunt needle.[5] This was facilitated by the absence of negative epidural space pressure, believed to be caused by dural dimpling,[6] as the needle was open to the atmosphere and pressures within the epidural space could equilibrate. Thus the transdural pressure gradient was limited to the CSF pressure alone. For penetration of the dura (a relatively tough membrane) to occur there must be a substantial reactive force.[7] This force is composed of the elastic recoil of the dura itself plus the transdural pressure gradient. In our cases the epidural space was open to air; thus the transdural pressure gradient was solely that of the CSF pressure, whereas elsewhere,[8] when a closed system was used, substantial negative pressures were seen at the moment of dural puncture. This created a substantial transdural pressure gradient and facilitated dural puncture. The low transdural pressure gradient in these cases appears to have conferred a margin of safety, albeit unwanted, against dural puncture. If this is true, then for those techniques which utilise intermittent application of positive pressure on a syringe, the insertion of a one-way valve designed to allow free ingress of air, while maintaining the ability to produce positive pressure between the Tuohy needle and the loss-of-resistance device may decrease the likelihood of inadvertent dural puncture (Fig. 3). This is achieved by reducing the transdural pressure gradient should dural tenting occur. When epidural placement has been achieved the valve could be removed for any aspiration tests required.

In eight of the subjects, aspiration produced CSF flow. It is not possible to say whether the aspiration caused puncture of the dura or just revealed it, but the suspicion remains that aspiration of a Tuohy needle may cause dural puncture by increasing the transdural pressure gradient. In three subjects, rotation caused CSF flow. Again the same suspicions are aroused that rotation can cause dural puncture.[7] Both these manoeuvres are part of routine clinical practice. The question arises as to whether they are essential.

CSF flow was reported as 'fast' in 21 patients and 'slow' in eight. The moderate hyperventilation during anaesthesia may have produced a small reduction in CSF pressure from

their baseline state, but elsewhere when measured we have found CSF pressures to be normal or moderately elevated.[8] It is commonly said that puncture of the dura with a Tuohy needle will produce an unmistakable 'fast' flow of CSF. However, in eight of our cases the rate of CSF flow could have been confused with the reflux of saline had loss of resistance to saline been used to identify the epidural space. The success of the Racz catheter when the Portex failed may simply reflect persistence or may be because of the exceptionally flexible tip of the former.

In conclusion, we have reported our observations during deliberate puncture of the dura with a Tuohy needle. The most striking finding was the distance from identification of the epidural space to puncture of the dura. We postulate that this is because of tenting of the dura by the blunt Tuohy needle. This is facilitated by the absence of negative epidural space pressure because of the use of an open system which allows time for pressure equilibration, thus minimising the reactive forces across the dura and conferring an unwanted margin of safety. Inclusion of a one-way valve between the loss-of-resistance device and the Tuohy needle may help to reduce the incidence of accidental dural puncture in clinical practice. We also found that aspiration and rotation of the needle revealed dural puncture in some cases, with the dura tented. Both these manoeuvres are part of normal clinical practice and their continued use may be questioned.

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Observations on deliberate dural puncture with a Tuohy needle: pressure measurements

R. J. TELFORD AND T. E. HOLLWAY

Summary

Pressure recordings were made during passage of a Tuohy needle from the interspinous ligament to the subarachnoid space for lumbar drain insertion. Epidural space pressures were always positive. Negative pressures were seen only at the moment of entry into the subarachnoid space. These were artefactual and were caused by tenting of the dura by the blunt Tuohy needle. Use of a closed measurement system such as this facilitates the development of large transdural pressure gradients because of the inability of the epidural space pressure to equilibrate with atmospheric pressure. This may contribute to ease of dural puncture.

Key words

Complications; dural puncture.
Equipment; Tuohy needle.

The use of lumbar cerebrospinal fluid (CSF) drainage to improve the operating conditions for intracranial aneurysm surgery has been routine in our institution for a number of years. The insertion of these drains has moved into the domain of the anaesthetist. Continuous measurements of pressure were made during the insertion of the Tuohy needle from skin to subarachnoid space. This paper describes our method of pressure measurement and our findings.

Methods

Patients requiring lumbar CSF drainage who presented to one of the authors (T.E.H.) during the period January 1989 to July 1989 were included. Dural puncture was performed with a Tuohy needle with the patient in the left lateral position under general anaesthesia after the routine monitors had been placed. A midline approach was used to the L_{2-3} or L_{3-4} interspace in all cases. Before insertion, the Tuohy needle was connected via a 3-way stopcock to a constant flow device (Graseby Medical Syringe Pump MS2000, capable of delivering 0.1–100 ml/hour and generating pressures in excess of 300 mmHg, the upper limit of our pressure measurement system) delivering 100 ml normal saline per hour and a pressure transducer (Medex MX807) calibrated from −40 mmHg to 300 mmHg (Fig. 1). The pressure values were displayed on a chart recorder (TOA EPR-152A Electronic Polyrecorder). The Tuohy needle was advanced steadily through the skin and spinal ligaments, until the epidural space was entered, as shown by a precipitous decrease in the displayed pressure. The infusor device was then immediately reset to a flow of 1 ml/hour and a short record made of epidural space pressure with the needle stationary. The needle was then advanced steadily until dural puncture occurred (usually indicated by a palpable click). A further short record of CSF pressure was made. Confirmation of subarachnoid needle placement was made by demonstrating free flow of CSF; the epidural catheter was then inserted into the subarachnoid space and the needle withdrawn.

Results

Eight patients were included in the study. Evaluation of their pressure-time recordings show the increasing pressures seen during passage through the interspinous ligament, the 'false' loss of resistance that may occur within this ligament, the high pressure generated during passage through the ligamentum flavum, and the precipitous decrease on entering the epidural space (Fig. 2). Epidural space pressures and CSF pressures are seen. Both respiratory and cardiac oscillations are easily visible (Fig. 3).

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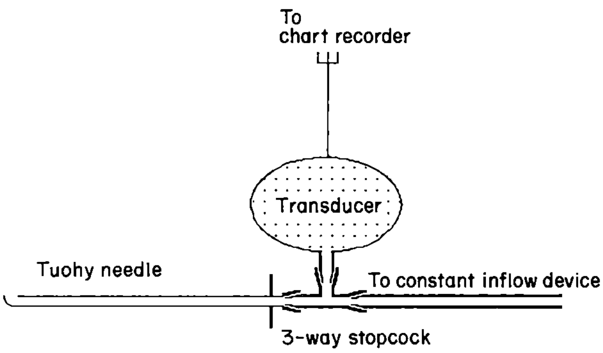

Fig. 1. The manometry system used.

The pressures found in each patient are shown in Table 1. Mean resting epidural pressures were all positive in the range 4–15.2 mmHg with a respiratory swing of 0.95–3.0 mmHg. No negative pressures were recorded in the epidural space when the needle was stationary. Resting CSF pressures were in the range 8.4–23.3 mmHg, (normal range 5.25–14 mmHg) with a respiratory swing of 1.20–5.0 mmHg. The gradient between resting epidural and CSF pressures was between 1.7 and 15 mmHg. Negative pressures occurred solely during the moment of dural puncture. These pressures were in the range −17 mmHg to greater than −40 mmHg; the latter figure represented the lowest pressure within the range of our transducer. Thus, in seven of the eight patients studied, at the moment of dural puncture, the greatest contribution to the reactive forces acting across the dura was the artefactual negative epidural space pressure.

Discussion

Most workers are in agreement that the measurement of a negative lumbar epidural space pressure is an artefact produced by tenting of the dura with a relatively blunt needle. Over the years the pressure within the lumbar epidural space has been measured by a variety of methods

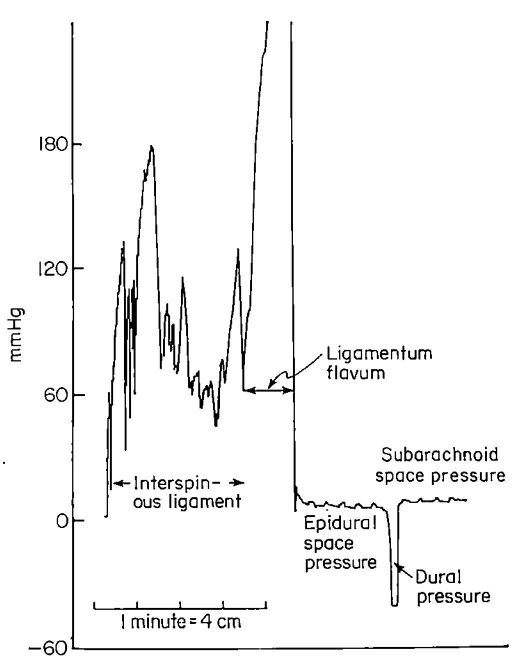

Fig. 2. A typical pressure, compared with time, recording.

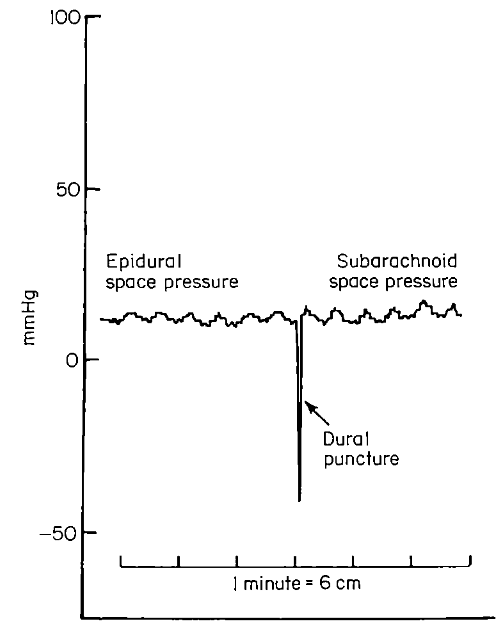

Fig. 3. Record of epidural and subarachnoid space pressures. Respiratory and cardiac oscillations can clearly be seen.

from simple water manometry,[1] to electromanometry.[2] Since the negative epidural space pressure is generated from a small volume source created by local dimpling of the resilient dura within the rigid walls of the spinal canal, it is essential to use a measuring system which undergoes a large pressure change for a given change in volume. This is why workers utilising measuring systems filled with liquids of high specific gravity (e.g. mercury) have recorded larger negative pressures than those utilising liquids of low specific gravity (e.g. water).[3]

In all cases we only observed negative pressures at the moment of entry into the subarachnoid space, while with the needle stationary, epidural space pressures were positive in the range 4–15.2 mmHg. The respiratory swing was of the order of 0.95–3.0 mmHg. In each case this was insufficient to render the epidural space pressure negative at any stage in the respiratory cycle. It is unlikely that conversion to spontaneous respiration, with its associated negative intrapleural pressures, would be enough to render these resting epidural space pressures negative, since it is only large changes in intrathoracic pressure that are transmitted to the lumbar epidural space.[4]

It is not possible to quantify absolute values for the negative pressures produced at the moment of dural puncture in all cases, since the pressures sometimes went off scale on the chart recorder. However, it is possible to speculate that, when utilising a closed system such as this, the negative epidural pressures were large enough to produce transdural pressure gradients of an order of magnitude that would assist the Tuohy needle in puncturing the dura. A one-way valve, as described elsewhere,[5] which would allow free ingress of air and prevent the epidural space pressure becoming subatmospheric, may confer some protection against inadvertent dural puncture, by minimising the transdural pressure gradient.

The measuring technique described may be modified to allow monitoring of trainee epiduralists; the syringe driver and tubing were replaced by syringe, saline and trainee. There are often occasions when loss of resistance occurs

Table 1. This indicates the pressures recorded in all eight patients (transdural pressure gradient = CSF pressure + greatest negative pressure recorded).

Patient	Epidural pressure (mmHg)		CSF pressure (mmHg)		CSF to epidural pressure gradient (mmHg)	Greatest negative pressure recorded (mmHg)	Transdural pressure gradient (mmHg)
	Mean	± swing	Mean	± swing			
1	10.0	2.10	14.0	2.75	4.0	> −40.0	> 54.0
2	4.0	1.50	10.0	2.00	6.0	−33.0	43.0
3	8.3	3.00	23.3*	5.00	15.0	−17.0	40.3
4	10.0	1.25	23.3*	1.80	13.3	−35.0	58.3
5	6.4	1.10	9.0	1.20	2.6	> −40.0	> 49.0
6	6.7	0.95	8.4	1.25	1.7	> −40.0	> 48.4
7	10.8	2.10	13.0	2.50	2.2	> −40.0	> 53.0
8	15.2	2.85	19.0*	3.35	3.8	> −40.0	> 59.0

*indicates elevated CSF pressure.

during the placement of the needle in the epidural space and there is some confusion as to whether the tip of the needle is in the epidural space or not. In the absence of cardiac or respiratory oscillations it is highly unlikely that this is the case.

In conclusion, we have used electromanometry to study the pressures generated during deliberate dural puncture with a Tuohy needle. Epidural space pressures were always positive with the needle stationary in the epidural space. Negative pressures were observed only on entry into the subarachnoid space. These are artefactual and are caused by tenting of the dura by the relatively blunt Tuohy needle. Use of a 'closed system' as a loss-of-resistance device facilitates the development of large transdural pressure gradients, because of the inability of the epidural space pressure to equilibrate with atmospheric pressure. This pressure gradient may be a contributing factor in accidental dural puncture. The inclusion of a one-way valve into the system to allow equalisation with atmospheric pressure may confer some degree of protection in this regard.

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A survey of secondary transfers of head injured patients in the south of England

H. A. L. VYVYAN, S. KEE AND A. BRISTOW

Summary

A survey by questionnare was carried out to look into the provision of facilities for the secondary transfer of head injured patients, as well as difficulties encountered. An 84.6% response rate was achieved from 110 hospitals in six regions in the south of England. The results showed that 21% of hospitals had been unable to make a transfer in the previous year, and delays were commonly experienced by 23.7% of hospitals. The nursing attendance during transfer was satisfactory, but the quality of medical escort was poor, and the standard of monitoring equipment available was unacceptable. Methods of improving the situation include implementation of the recommendations of the Royal College of Surgeons, as well as the Association of Anaesthetists' recommendations for standards of monitoring and provision of intensive care.

Key words

Complications; trauma.

The incidence of significant head injury has been quoted as high as 300 per 100 000 of the population per year.[1] In most instances, such cases are admitted to the nearest acute unit and then transferred to a neurosurgical centre if warranted. Following our experience in both district general hospitals and our own neurosurgical centre, a study was undertaken to examine the standard of care provided in transit.

Methods

A postal questionnaire was sent to the anaesthesia or accident and emergency departments of each hospital in six Regional Health Authorities in the south of England (North East Thames, South East Thames, North West Thames, South West Thames, East Anglia and Wessex) which receive acute admissions, but do not have neurosurgical facilities on site. These units would be expected to be the origin of secondary transfers of serious head injuries to regional neurosurgical centres.

A copy of the questionnaire is shown in Figure 1. Each hospital was questioned about the number of head injuries transferred in the last year, the equipment and staff sent to escort the patients and any delays or problems that had been encountered. Those who did not reply were sent another questionnaire and nonresponders were contacted by telephone.

Results

The response rate was 84.6% (93 out of 110 questionnaires). The number of head injuries transferred to regional neurosurgical centres varied, but over half the respondents had sent more than 10 patients during the previous year (Table 1). Twenty-three hospitals (24.7%) were unable to transfer one or more patients during this period. The reasons given are shown in Table 2. One hospital encountered all of these reasons, and another gave two reasons.

The indications for transferring patients are shown in Table 3. Thirty-one hospitals (33.3%) were able to perform their own computerised tomography (CT) scans, although three admitted to being unable to staff their scanners after 1700 hours or at weekends.

Monitoring and therapeutic equipment normally available to the respondents is shown in Table 4. No hospital had every item and only three hospitals (3.2%) had comprehensive monitoring (items 1–5). One hospital only

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Fig. 1. The questionnaire.

1. How many head injuries have been transferred from your hospital in the last year?
   - 0–5
   - 6–10
   - 11–20
   - over 20
2. Were you unable to transfer any head injuries?
3. If so, what were the reasons?
   - Lack of beds
   - No ambulance
   - Lack of nurses
   - Lack of doctors
   - Patient too sick
   - Other (please specify)
4. What equipment do you normally have available for transfer?
   - Electrocardiograph
   - Noninvasive blood pressure
   - Invasive blood pressure
   - Pulse oximetery
   - Capnography
   - Ventilator
   - Infusion pumps
5. What staff do you normally send?
   - Anaesthetic senior registrar
   - Anaesthetic registrar
   - Anaesthetic senior house officer
   - Surgical senior registrar
   - Surgical registrar
   - Surgical senior house officer
   - Intensive care nurse
   - Accident and emergency nurse
   - Ward nurse
   - Whoever is available
6. Why do you normally transfer head injuries?
   - Scanning
   - Neurosurgical intervention
   - Insufficient intensive care beds.
   - Other (please specify)
7. How often do you experience a delay?
   - Rarely
   - Commonly
   - Almost always
8. Is this due to?
   - Finding a bed
   - Finding staff
   - Finding equipment
   - Waiting for an ambulance
   - Traffic congestion
   - Other (please specify)
9. What other problems have you encountered?

Table 1. Numbers of head injuries transferred to neurosurgical centres in the last year.

Number of transfers	Number of hospitals ($n=93$)	%
5 or less	23	24.7
6 to 10	20	21.5
11 to 20	30	32.5
Greater than 20	20	21.5

Table 2. Reasons why patients could not be transferred.

	Number of hospitals
Lack of beds in regional neurosurgical centre	15
Lack of doctors	1
Lack of nurses	1
Lack of ambulance	3
Condition of patient too critical	7
Administrative difficulties in regional centre	2

had an electrocardiograph available and 13 hospitals had no means of measuring arterial blood pressure in transit. A greater proportion of the hospitals who transferred more than 20 patients in the previous years had ventilators, noninvasive blood pressure cuffs and pulse oximetry, but this was not statistically significant (Chi-squared tests with Yates' correction).

All respondents sent medical staff to escort the patient (Table 5). Five hospitals normally sent medical staff other than anaesthetists, of which two used medical senior house officers (SHOs), two surgical SHOs and one accident and emergency SHOs.

Nearly a quarter of hospitals commonly experienced delays whilst transferring patients (Table 6). There was no correlation between the frequency of delays and the number of patients transferred. The reasons for delay are shown in Table 7. In addition, there were complaints that staff experienced long delays waiting for transport to return them and the equipment back to the hospital after transfer.

Discussion

In 1986 the Royal College of Surgeons of England's Working Party on head injuries noted the value of early admission to a neurosurgical unit and the importance of CT scanning.[2] Specific guidelines for initial management after head injury had already emphasised the early use of CT scanning for patients at risk of intracranial haematoma.[3]

This study demonstrates that 2 years later, not only are large numbers of head injuries still needing to be transferred to regional neurosurgical centres after admission to a district general hospital, but that 66.6% of these hospitals do not have CT scanning. Over 20% of these hospitals were frequently delayed undertaking transfer, suggesting that current transport arrangements are inadequate. Most importantly, transfers that were clinically necessary were unable to be undertaken, and in only 30% was this the result of the patient's clinical condition. As head injuries are most commonly seen in young productive patients,[1] this

Table 3. Reasons for secondary transfer.

	Number of hospitals	%
Computerised tomography and neurosurgical intervention	62	66.6
Neurosurgical intervention only	31	33.3
Additional reasons		
Lack of intensive care beds	3	3.2

Table 4. Equipment normally available for transfer.

	% of all responders ($n=93$)	% of those hospitals who transferred less than five patients in the previous year ($n=23$)	% of those hospitals who transferred more than 20 patients in the previous year ($n=20$)
Electrocardiograph	100.0	100.0	100.0
Noninvasive blood pressure	76.3	65.2	75.0
Invasive arterial blood pressure	22.6	30.4	20.0
Pulse oximeter	61.3*	60.9	75.0*
Capnograph	5.4	4.4	5.0
Ventilator	69.9	56.5	75.0
Infusion pump	77.4	87.0	60.0

*Includes two hospitals where pulse oximeter only available some of the time.

must be considered to be an unacceptable situation, both in terms of human suffering and loss to the economy.

In 1988 the Royal College of Surgeons' report on the management of patients with major injuries[4] noted that up to 30% of deaths were preventable if the patients had been managed in trauma centres with full facilities, and recommended that patients with life-threatening injury beyond the facilities or capabilities of a district general hospital should be transferred to a centre established at regional or multidistrict level. They proposed that access to a trauma centre would be by 'high quality interhospital transfer using a specially equipped ambulance or helicopter staffed with experienced medical personnel, or, by direct referral from the scene of the accident'. Our paper supports such a recommendation, since these facilities would have overcome the delay which 20 hospitals reported whilst waiting for equipment and staff, and also the first three reasons why patients could not be transferred (Table 2).

The Association of Anaesthetists of Great Britain and Ireland has made recommendations regarding minimum standards of monitoring during anaesthesia and recovery.[5] This document states that when patients are being transferred under the care of the anaesthetist from one part of the hospital to another or from one hospital to another, similar requirements obtain. We support this statement, and believe that appropriate monitoring for transfer of the head injured patient should be no less than that required for the anaesthetised patient in an operating theatre, and if anything, should be more intense. The survey showed that only 3.2% of sending hospitals meet these standards, in that only three hospitals had a pulse oximeter, electrocardiograph, capnograph, invasive and noninvasive blood pressure monitoring available for secondary transfer of serious head injuries.

Forty percent of hospitals were unable to monitor oxygen saturation during transport. This is of some concern since the patients are often critically ill, and arterial desaturation is difficult to estimate visually,[6] particularly in a moving ambulance, and often at night. Pulse oximetry has been strongly recommended for use during transport.[7]

As expected, few respondents (5.4%) had a capnograph, which may be because of the lack of capnographs which are small, battery powered and free from sampling obstruction. Capnography is recommended as a means of continuously monitoring the anaesthetised patient,[5] and we believe it is important for monitoring the head injured patient during transfer: it provides a ventilator disconnect alarm, as well as portraying information in the waveform. The end-tidal carbon dioxide tension allows the anaesthetist to avoid hypoventilation and achieve adequate hyperventilation to reduce intracranial pressure. It is hoped that the introduction of more suitable capnographs will lead to their greater usage for transfers.

Table 5. Standard of staff normally sent.

	Number of hospitals	%
Medical staff		
Anaesthetic senior house officer	55	59.1
Anaesthetic registrar	30	32.3
Anaesthetic senior registrar	1	1.1
Anaesthetic consultant	2	2.1
Other	5	5.4
Nursing staff		
Accident and emergency or intensive care unit nurse	89	95.7
Ward nurse	3	3.2
None	1	1.1
Addditional staff		
Operating department assistant	3	3.2

Table 6. Regularity of delays during secondary transfer.

	Number of hospitals ($n=93$)	%
Almost always delayed	4	4.3
Commonly delayed	18	19.4
Rarely delayed	71	76.3

Table 7. Reasons for delay during secondary transfer.

	Number of complaints by respondents
Delay in neurosurgical acceptance of patient	6
Difficulty finding a bed	23
Finding staff to accompany a patient	14
Finding transferring equipment	6
Delay obtaining ambulance	22
Breakdown of ambulance in transit	2
Traffic congestion	7
Deterioration of patient's condition in transit	1
Delay on arrival at regional centre	18

We believe it unacceptable that 13 hospitals (14%) had no means to measure blood pressure in transit. Only 22.6% of hospitals had invasive (intra-arterial) blood pressure monitoring, despite a survey in 1987 which revealed a similar figure and suggested that it be more widely adopted for the transport of critically ill patients.[8] There is evidence that noninvasive measurements are unreliable in transit,[9,10] and invasive monitoring has been shown to be attainable.[11]

Medical staff who escort head injuries must have skill in the management of tracheal intubation, airway and respiratory problems, cardiovascular monitoring and support and drug administration.[8,12] Cardiorespiratory complications may occur during transport,[13–15] and have been shown to be more common in the presence of junior doctor and nonanaesthetist escorts.[16] Five hospitals sent SHO grade doctors who were not anaesthetists, who in our opinion cannot meet the above mentioned requirements. 59.1% of hospitals sent the most junior grade of anaesthetist, and some of these SHOs would be newly trained and inexperienced in the care of critically ill patients. We would expect a patient with serious head injuries to be treated in hospital by at least a registrar, and it is the protocol of our unit for postfellowship registrars to manage such cases. We believe that this standard of medical supervision should be maintained during transfer, but we recognise that transfers occurring outside normal working hours may leave many hospitals deprived of the senior resident anaesthetist for a considerable time, which in itself is unsatisfactory.

A report by the working party of the Association of Anaesthetists, which examined intensive care services in the United Kingdom,[17] recommended that the movement of patients to regional centres should be the responsibility of the receiving unit. The implementation of this proposal, and the attachment of transfer schemes with clearly defined staff and equipment to regional centres, would overcome many of the inadequacies in secondary transfer demonstrated by our survey. Current transfer schemes such as the Clinical Shock Study Group in Glasgow and Barts Careflight remain the exception despite demonstrating that these proposals can be achieved. It is advantageous to be able to transport these patients rapidly over large distances since 15 hospitals (16.1%) were unable to transfer patients because their local centre was full. Proper utilisation of our national bed finding system would also reduce the delays due to difficulty finding beds experienced by 23 hospitals (24.7%).

Twenty percent of hospitals reported delay on arrival at the regional centre, and this needs to be urgently overcome, not only to avoid further delay in patient treatment, but also because battery powered equipment and portable oxygen cylinders cannot function indefinitely.

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Continuous thoracic epidural fentanyl for post-thoracotomy pain relief: with or without bupivacaine?

K. A. GEORGE, P. M. C. WRIGHT AND A. CHISAKUTA

Summary

Twenty-five ASA 1 or 2 patients undergoing thoracotomy were entered into a prospective, randomised, double-blind study comparing thoracic epidural fentanyl alone and thoracic epidural fentanyl combined with 0.2% bupivacaine. Pain relief, pulmonary function and cardiovascular stability were assessed. Pain relief was superior in the bupivacaine series ($p < 0.05$) during the first day after operation and this was accompanied by better oxygenation ($p < 0.05$); the difference did not persist into the second day. Forced expiratory variables were reduced in both series to 50–60% of the values before operation throughout the study ($p < 0.05$) and differences did not occur between the groups. The incidence of side effects attributable to epidural fentanyl was high, but hypotension did not occur. Small doses of bupivacaine administered together with fentanyl into the thoracic epidural space improve analgesia without causing hypotension.

Key words

Anaesthetic technique regional; epidural.
Analgesics; fentanyl.
Anaesthetics; local bupivacaine.

Lateral thoracotomy results in severe pain and deleterious changes in pulmonary physiology.[1] Shallow breathing during the first day following surgery can lead to atelectasis, pulmonary collapse and hypoxia[2] which may continue for some days. Effective postoperative analgesia and physiotherapy can modify this sequence, inhibit changes in forced expiratory variables and prevent the onset of hypoxia.[3] Postoperative pulmonary function is still reduced even with epidural opioid or local anaesthetic treatment.[4,5] Opioid agents produce no further improvement when given after local anaesthetics,[5] but the effect of local anaesthetics after epidural opioid treatment remains to be evaluated.

Epidural opioid administration provides good postoperative analgesia,[6] and has been used successfully to treat pain and improve pulmonary mechanics after chest trauma.[7] Epidural local anaesthetics can also produce effective analgesia, but after thoracic surgery there is considerable risk of hypotension.[8] While a combination of local anaesthetic and opioid improves the quality of pain relief,[9] the problem of cardiovascular instability remains.

The purpose of this study was to compare the effect of an epidural infusion of a dilute bupivacaine/fentanyl mixture, against epidural fentanyl alone on pain, cardiovascular stability and postoperative pulmonary function after thoracic surgery.

Patients and Methods

This study was carried out with the approval of the local medical ethics research committee and with informed patient consent. Adult patients of ASA status 1 or 2 undergoing lateral thoracotomy were studied. Patients undergoing pneumonectomy were excluded.

The patients were premedicated with temazepam 10 mg. In the theatre, after placement of peripheral venous and radial artery catheters, an epidural cannula was placed at either the T_4–T_5 or T_5–T_6 intervertebral space with 3 cm of the cannula left in the epidural space. Fentanyl 100 μg and bupivacaine 20 mg in a total volume of 10 ml were injected, and after 15 minutes the upper and lower levels of sensory block were determined using a cold stimulus (ethyl chloride spray). Anaesthesia was induced with thiopentone, sufficient to obtund the eyelash reflex, muscle relaxation achieved with atracurium and a left sided double lumen tube (Bronchocath, Mallinkrodt) placed in the trachea.

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Maintenance anaesthesia was with isoflurane in nitrous oxide and oxygen. One-lung ventilation was performed when required.

After the operation, extubation took place in the operating theatre, and the patients were transferred to the intensive care unit (ICU). Here they were randomly allocated to one of two treatment groups: a saline group to receive continuous epidural fentanyl only and a bupivacaine group to receive bupivacaine in addition to the epidural fentanyl. Coded 10 ml ampoules were supplied by the hospital pharmacy containing either sodium chloride 0.9% or bupivacaine 0.25%. These were mixed in a ratio (v:v) of 4:1 with fentanyl 50 μg/ml. The saline group received fentanyl 10 μg/ml in saline and the bupivacaine group fentanyl 10 μg/ml in bupivacaine 0.2%.

Each patient received 5 ml of the test solution, via the epidural cannula, on admission to the intensive care unit, and subsequently a continuous epidural infusion was commenced at 5 ml/hour. The infusion was adjusted according to the quality of analgesia: if analgesia was complete the infusion was reduced in stages to 3 ml/hour, if analgesia was inadequate the infusion rate was increased to a maximum of 5 ml. Additional analgesia was administered if requested by the patient. This consisted of 3 ml of the test solution injected epidurally if the pain was in the region of the wound, or intravenous morphine 2.5 mg if the pain was remote from the wound e.g. shoulder tip pain. The patients remained in the ICU for a minimum of 48 hours after the operation. All received continuous 40% humidified oxygen at 5 litres/minute (Aquapak). Physiotherapy was performed once on the evening after the operation, and three times the day after. On the day after the operation patients were encouraged to sit in a chair for short spells.

Measurements

On the day before operation, pulmonary function was assessed by measurements of forced expiratory volume in the first second (FEV_1) and forced vital capacity (FVC) using a pneumotachograph-based vitalograph (Alpha, Vitalograph Ltd) and peak expiratory flow (PEF) using a mini Wright respirometer. Measurements were made with the patient semirecumbent in bed in a similar position to that expected after operation. Patients were instructed in the technique before measurements were made, and were familiarised with the visual analogue scoring system. Arterial blood was taken for blood gas and pH analysis (Corning 168), and baseline cardiovascular variables determined. After the operation, at 2 and 6 hours and subsequently every 6 hours until 48 hours, repeated assessments of pain, PEF, FVC, FEV_1 and arterial blood gas analysis were made. Specific periods during the second day were allocated to allow for sleep. Pain relief was assessed using serial 100 mm visual analogue scores (VAS), extremes were labelled 'no pain' and 'the worst possible pain'. These were recorded by one of the investigators on all occasions, and in such a way that the patient was blind to his (her) previous responses. In addition, cardiovascular stability was assessed by serial measurements of heart rate by ECG and arterial blood pressure by direct intravascular measurement.

The total volume of analgesic solution administered over the 48-hour period of the study was noted, as was the number of epidural or intravenous boluses of either test solution or morphine. The incidence of itching, nausea, vomiting, complaints of numbness or limb weakness were noted specifically at each assessment. The patients were not routinely catheterised and the necessity for postoperative bladder catheterisation was recorded.

Unless otherwise stated data are presented throughout as the mean with 95% confidence intervals. Statistical analysis was carried out using Chi-squared test for frequency data and one-way analysis of variance for parametric data. In order to avoid multiple significance testing, data from 2, 6, 12, and 18 hours after recovery are combined and considered as day one and the remaining time points are considered as day two. Each variable was meaned for each patient on a given day.

Results

Twenty-five patients were entered into the study but four patients were withdrawn for reasons unrelated to the investigation. One patient from each group was subject to reoperation because of continued bleeding, and in two the epidural cannula became displaced but this was not noted until some time had elapsed. Of the remaining 21 patients 11 received saline and 10 received bupivacaine. The two groups were broadly comparable in age, weight, height, and for other variables recorded before the operation (Table 1). The initial block assessed at the beginning of the operation was similar in the two groups, from T_2–T_4 to T_7–T_9 in all the patients.

Pain scores were greater in the saline group during the first day ($p < 0.05$); pain was worst at 6 hours after recovery in both the groups (Fig. 1). Analgesic failure (defined as VAS for pain > 30 mm) occurred at some point during the first day in six of the saline series and none of the bupivacaine series ($p < 0.05$). Pain scores on the second day after operation were similar; two and one patients in the saline and bupivacaine groups respectively had analgesic failure at some time during the day. The total volume of test solution administered was 173 ml and 147 ml in the saline and bupivacaine groups respectively (NS), and intravenous morphine was administered to four and two patients in the saline and bupivacaine groups (NS).

Heart rate (HR) changes were almost identical in the two series during the period of the study (Fig. 2). Systolic arterial blood pressure (SAP) decreased from 142 to a minimum of 123 and from 142 to a minimum of 123 at 18 hours after operation in the saline and bupivacaine groups respectively. Although during the first day the arterial

Table 1. Demographic characteristics and preoperative variables mean (95% CI).

	Bupivacaine (n = 10)	Saline (n = 11)
Age; years	46 (38–54)	46 (34–58)
Weight; kg	59 (54–64)	64 (58–70)
Height; cm	167 (161–173)	170 (165–175)
M:F	7:4	4:6
SAP; mmHg	142 (131–153)	142 (130–154)
HR; beats/minute	76 (70–82)	76 (71–81)
PEF; litres/minute	398 (333–463)	421 (444–498)
FEV_1; litres	2.29 (1.72–2.82)	2.62 (1.98–3.26)
FVC; litres	3.13 (2.48–3.78)	3.58 (2.83–4.33)

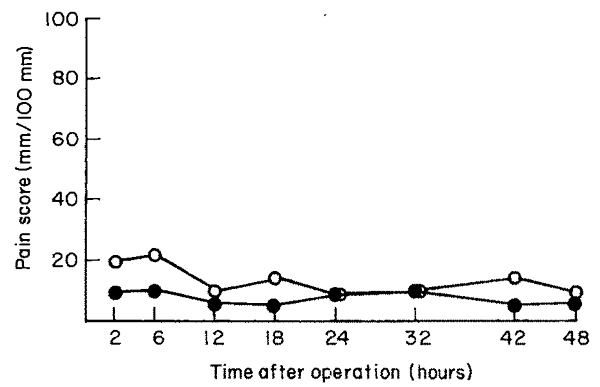

Fig. 1. Mean pain scores during the 48 hours after operation. ●, bupivacaine; ○, saline.

blood pressure was less in the bupivacaine group compared to the saline group the differences were not significant; the mean minimum systolic arterial blood pressure was 118 and 116 in the saline and bupivacaine groups respectively. Hypotension did not occur, even when patients sat out of bed on the second day, and no active measures were required in any patient to maintain the arterial blood pressure during any part of the postoperative phase (Fig. 2).

There was a reduction in PEF, FVC and FEV_1 to 50–60% of the baseline value throughout the study ($p < 0.05$), but there were no significant differences between the groups (Fig. 3). Arterial pH was reduced in all patients immediately after the operation ($p < 0.05$) but recovered within 6 hours, and subsequently remained above 7.39 in all patients. Oxygenation was satisfactory in all patients during the study. However mean Pa_{O_2} was greater in the bupivacaine group during the first day ($p < 0.05$); it was 14.6 kPa and 12.05 kPa in the bupivacaine and saline groups respectively. The value of Pa_{CO_2} remained within

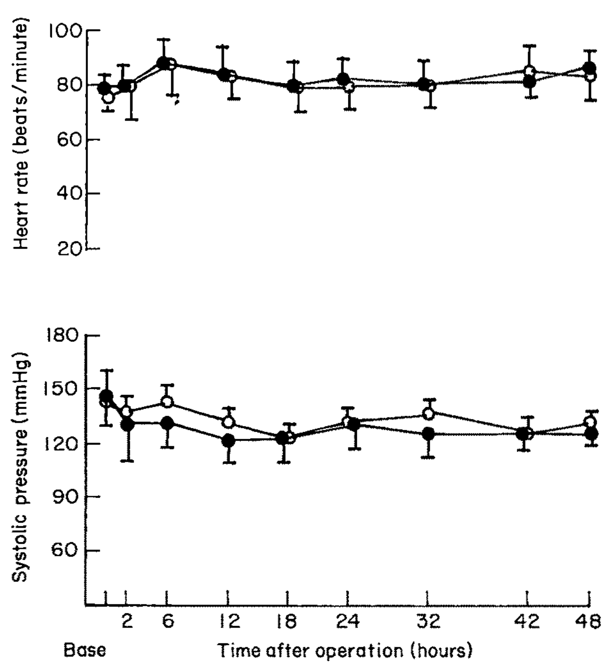

Fig. 2. Mean (95% CI) systolic blood pressure and heart rate at intervals after operation. ●, bupivacaine; ○, saline.

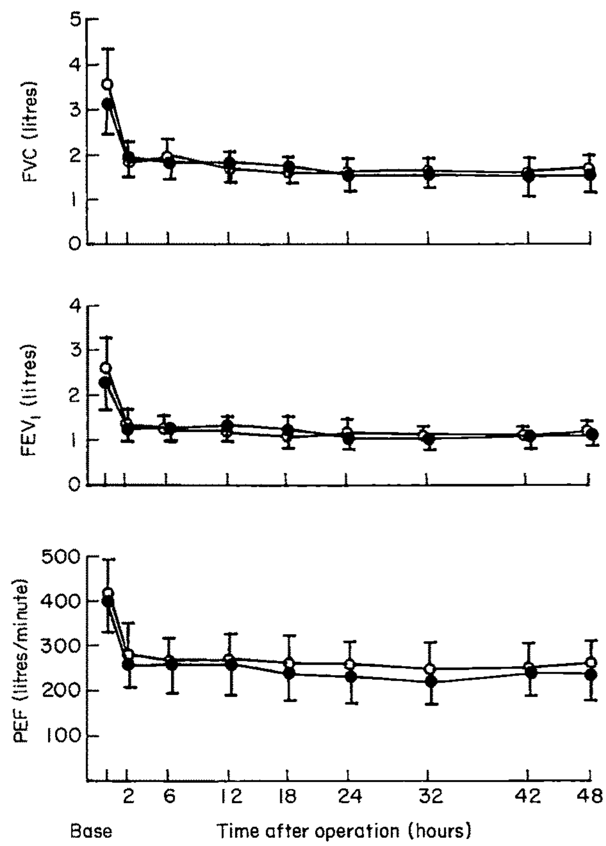

Fig. 3. Mean (95% CI) PEF, FVC and FEV_1 at intervals after operation. ●, bupivacaine; ○, saline.

Table 2. Adverse side effects.

	Bupivacaine (n = 10)	Saline (n = 11)
Emetic symptoms	5	6
Pruritus	5	5
Urinary retention	4	8
Numbness	3	2
Limb weakness	1	0

physiological limits throughout the study and there were no differences between the groups.

The incidence of emetic symptoms, itching and urinary retention were all approximately 50% and were similar in the two groups. The incidence of limb weakness or numbness of the trunk was low in both groups (Table 2).

Discussion

Thoracic epidural fentanyl infusion is an effective method of relieving pain after thoracotomy,[12] and compares favourably with cryo-analgesia. This study demonstrates that improved pain relief can be obtained by the addition of small (6–10 mg/hour) doses of bupivacaine to an infusion of fentanyl. The cost in terms of side effects appears to be slight. In particular, postoperative hypotension did not occur during the conduct of this investigation and the incidence of itching, emetic symptoms, and urinary retention was unaltered. The addition of this dose of bupivacaine did not prevent early mobilisation.

When epidural local anaesthetics are used alone to provide pain relief after either thoracic[8,11,13] or upper abdominal surgery,[5,14] analgesia is frequently unsatisfactory and often accompanied by hypotension, with an incidence of up to 80% in a post-thoracotomy series.[8] Although some authors report better results,[15,16] thoracic epidural fentanyl is generally more satisfactory; it provides analgesia without hypotension after thoracic surgery,[12] blunt chest trauma,[7] and upper abdominal surgery.[4,17] If a low concentration of bupivacaine (0.1%) together with morphine is administered in a larger volume than that used here, pain relief following thoracotomy is improved[11] but at the cost of a 20% incidence of hypotension. Hypotension also occurs if a small (6 ml/hour) volume of 0.5% bupivacaine is administered together with morphine.[5] The present study confirms better analgesia occurs when bupivacaine 0.2% is combined with fentanyl, but without hypotension. Circulatory changes after thoracic epidural bupivacaine 25 mg include a reduction in heart rate, arterial blood pressure and cardiac output;[18] part of the effect is due to systemic absorption. We can only suggest that the absence of hypotension during our study may be explained by the very small dose used (maximum dose 10 mg/hour), in a maximum volume of 5 ml/hour, minimising spread in the epidural space.

The level of pain experienced by both groups in this study was very low; the mean pain score of the fentanyl only group was above 20 mm only at 6 hours after operation, at which point it was 21 mm. This contrasts with the work of Gough and coworkers where mean pain scores were never below 20 mm during the first 2 days after operation.[12] There are many possible methodological explanations for this difference, but the most outstanding difference between the two studies was that in our series the analgesic regimen commenced before operation. Better analgesia when total nociceptive input is reduced has been noted before and explained on the basis of reduced plasticity changes in the central nervous system.[19]

Pain produces a restrictive pattern of ventilation. Vital capacity, often reduced postoperatively to about half of pre-operative values, and sometimes as low as 20%,[20] has been increased by a variety of analgesic techniques. Epidural opioid[4,6,21] and local anaesthetic[22] treatment have a greater beneficial effect on forced expiratory variables compared to the systemic administration of opioids. In one study the addition of morphine to epidural bupivacaine failed to produce any further improvement in forced expiratory parameters.[11] The authors suggested that the bupivacaine might reduce the power of the intercostal muscles. This study does not support such a hypothesis. It has long been recognised that there is a limit to the improvement in forced expiratory variables that can be sustained by pain relief in the postoperative patient,[23] and it would seem that the limit may be reached by either opioid or local anaesthetic drugs administered into the epidural space.

Patients in this study received 40% humidified oxygen, or more if it was clinically indicated. This would tend to minimise differences between the groups. Despite this the bupivacaine series were significantly better oxygenated during the first day after the operation. Epidural bupivacaine analgesia has been demonstrated previously to improve oxygenation compared to systemic morphine;[24] this improvement appears to be independent of changes in forced expiratory parameters. Although the differences in Pa_{O_2} were small, any therapeutic intervention capable of improving oxygenation is of great clinical significance.

The incidence of side effects attributable to epidural fentanyl (emetic symptoms, itching and urinary retention) was large compared to previous reports.[12] This might be the result of the greater frequency with which symptoms were elicited during this investigation. Numbness of the trunk (elicited only on direct enquiry) appeared in both groups and one patient in the bupivacaine group complained of slight weakness in one arm; this patient received the largest total volume of solution in the entire study. Comparison with other studies is difficult since reports of motor symptoms are often omitted, but the complete absence of symptomatic lower limb weakness is important for early mobilisation and is a reassuring finding.

In summary, the addition of small doses of bupivacaine to continuous thoracic epidural fentanyl improves analgesia and oxygenation in post-thoracotomy patients without producing hypotension. In a recent review of pain relief after thoracic surgery[1] it was concluded that a combination of techniques was likely to provide the most satisfactory outcome. The combination of dilute bupivacaine with a lipophilic opioid administered into the thoracic epidural space provides good quality analgesia with an absence of serious side effects.[25] The results of our study support the growing use of these techniques and we have now adopted the technique described as standard therapy after thoracic and upper abdominal surgery.

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CASE REPORT

The automatic implantable cardioverter-defibrillator

Implications for anaesthetists

C. M. E. CARR AND S. M. WHITELEY

Summary

This paper describes the anaesthetic management of a patient who had an automatic implantable cardioverter-defibrillator. The working principles of the device, the indications for its insertion and the postoperative complications, are discussed. An increasing number of cardioverter-defibrillators are being implanted in the UK. At least two general anaesthetics are required for each patient; one for implantation of the device and a second for testing its efficiency in terminating ventricular tachycardia and ventricular fibrillation. In future, the number of patients presenting for noncardiac surgical procedures is likely to increase, therefore every anaesthetist should be aware of the problems involved in management.

Key words

Heart; arrhythmias, electroconversion.
Anaesthesia; cardiovascular.
Equipment; automatic implantable cardioverter-defibrillator.

Ventricular tachyarrhythmias are a major cause of sudden death in Western society. Some patients who develop sustained but self-terminating ventricular tachyarrhythmias, in the absence of acute myocardial infarction, are at high risk from progressive cardiac failure and sudden death. Their one-year mortality rate is up to 40%.[1] After antiarrhythmic therapy has been initiated in these patients, a subgroup will emerge whose arrhythmias are not controlled or who are intolerant of the drugs prescribed. In these patients the possibilities for further treatment may include subendocardial resection, insertion of an automatic implantable cardioverter-defibrillator (AICD), or both. Specific indications for the choice of procedure are becoming clearer.[2] The first AICD was implanted into a human in 1980, after 10 years of animal studies.[3] The device has since been improved by refining the sensing and diagnostic algorithms and by the provision of a backup pacemaker facility. Several thousand patients in America have received AICD implants, and their outcome has been the subject of reviews.[4,5] Experience in the UK is much less extensive, but numbers are increasing. At the General Infirmary in Leeds, nine AICD devices were implanted from August 1989–November 1990.

The device in use at present is the Guardian 4202 Implantable Cardioverter Defibrillator (Telectronics Limited, Europe). Its weight is 282 g, dimensions 11 cm × 8 cm × 2 cm and it costs approximately £10 000. It may be implanted subcutaneously into either the abdomen or the thorax.

The device senses electrical activity using a bipolar pacing lead system. The intracardiac electrocardiogram (ECG) is converted to digital sensed events which are then classified according to the time interval between consecutive events. The device thus utilises interval data to differentiate tachycardias and is described as having a rate-based detection algorithm. The band rate of the tachyarrhythmias which the device will detect can be programmed. When six tachycardia counts are noted in any sequence of seven intervals, detection occurs and the defibrillator charges. A check that the tachycardia persists is then made at two further points; first of all, after a minimum delay of 6–20 seconds (programmable) and secondly, when the capacitors are fully charged, or 30 seconds, whichever is reached first. A shock is delivered to the patient via the two epicardial defibrillator patches, only if the tachycardia is reconfirmed at both these points. The device then automatically recharges to a higher energy level in preparation for a further shock, if required. The maximum number of shocks that can be delivered in any one series is programmable from four to seven. The fourth and subsequent shocks are delivered at 30 joules, regardless of the initial programmed energy. Any charge not required is dumped internally in the defibrillator.

Patients with the AICD *in situ* or in whom insertion is

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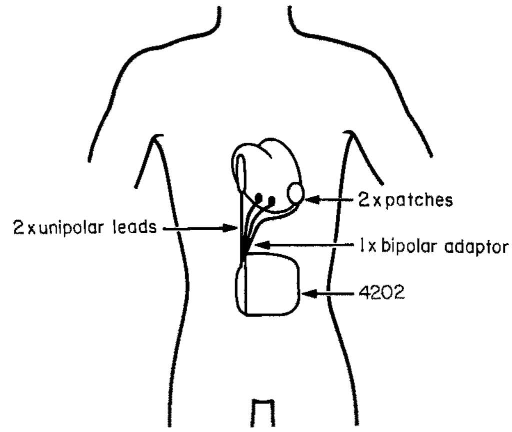

Fig. 1. The Automatic Implantable Cardioverter-Defibrillator (Guardian 4202). The implanted system.

planned may present to the anaesthetist in several ways, as shown by the following case history.

Case history

A 58-year-old man developed a monomorphic ventricular tachycardia (VT) during exercise testing, 6 weeks after sustaining an inferior myocardial infarction. He felt dizzy, but did not faint. Coronary angiography showed subtotal occlusion of his circumflex vessel with otherwise minor coronary artery disease. At subsequent electrophysiological testing, VT was easily induced and terminated by overdrive pacing without loss of consciousness. He first presented to an anaesthetist for assessment before undergoing a combined procedure of bypass grafting of the circumflex artery and left ventricular electrophysiological mapping. At operation it proved impossible to reach the demonstrated focus of VT without compromising the mitral valve, therefore two pericardial defibrillator patches were inserted. The ability of the patches successfully to shock the patient out of induced VT and ventricular fibrillation (VF) was confirmed, but the AICD was not inserted at this stage. Thirteen days later, during abdominal implantation of the AICD under general anaesthesia, VT and VF were induced to test the efficiency of the implanted system in terminating these arrhythmias.

Infection, which occurred at the abdominal implantation wound site, did not respond to antibiotic therapy. Thus 5 weeks after the first implantation, a third general anaesthetic was required for repositioning of the AICD into the

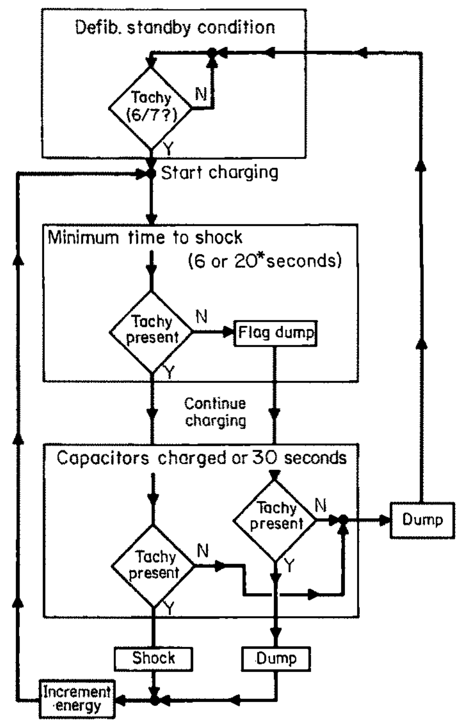

Fig. 2. The Automatic Implantable Cardioverter-Defibrillator (Guardian 4202). Flow chart of reconfirmation behaviour. Defib, defibrillator. Tachy, tachyarrhythmia. N, no. Y, yes. *Initial charge sequence only.

chest wall. Once again, this procedure included the deliberate induction of VF. After a further 15 weeks the patient was admitted for testing of defibrillator thresholds and function. He had not experienced any episodes of arrhythmia which required his AICD to fire and he had no other cardiac symptoms. His medication was naproxen, amiodarone, isosorbide mononitrate and co-amilofruse. After premedication with temazepam 20 mg, a left radial arterial line was inserted under local anaesthesia. Monitoring of ECG and direct arterial pressure was started before induction, which was with fentanyl 100 μg, etomidate 20 mg and vecuronium 6 mg.

The trachea was intubated and the lungs ventilated with oxygen 33% nitrous oxide 67% and enflurane 0.5–1%. Direct arterial pressure monitoring was continued, with ECG, pulse oximetry and capnography. All measurements were stable until an electrode wire was inserted into the right ventricle via the right femoral vein and VT/VF was induced.

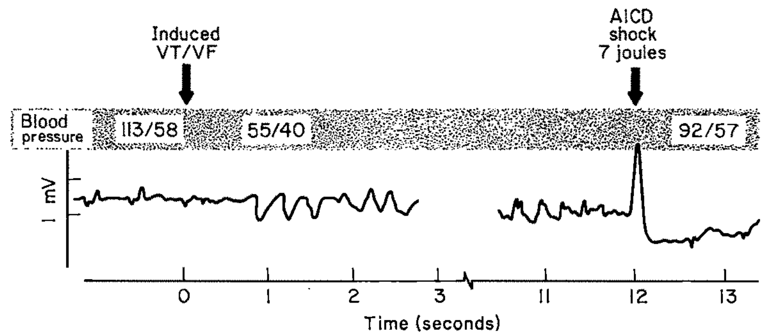

Fig. 3. ECG recording (lead II) taken at the time of induced VT/VF. A successful return to sinus rhythm following a single internal shock is recorded.

A real time printout of the ECG shows that satisfactory termination of the tachyarrhythmia was obtained by a single internal shock of 7 joules, delivered after 12 seconds. It is of note that during the period of this arrhythmia, peripheral perfusion was inadequate for pulse oximetry. The total time from induction to removal of the tracheal tube was 23 minutes.

The patient initially made an uneventful recovery but was readmitted to hospital a week later having had three episodes of inappropriate firing of the AICD, which caused him some discomfort. On each of these occasions, the patient had no symptoms before the device fired. The fault was traced to an oversensitive endocardial pacing lead, which was explored under local anaesthesia and corrected. However, 8 months after the AICD was reimplanted, infection and erosion at the new implant site required device removal. The patient still has easily inducible VT on electrophysiological testing, which renders him haemodynamically unstable. At present this reverses spontaneously after less than 30 seconds. His implant wound is healing and further AICD implantation remains a possibility.

Discussion

This case illustrates many of the problems which the anaesthetist may encounter in dealing with patients who have, or are scheduled to have, an AICD inserted. Patients presenting for AICD insertion will usually have coronary artery disease or, less commonly, an idiopathic cardiomyopathy or congenital heart disease. Their ventricular function, as assessed by ejection fraction, is often very poor,[4,6-12] and the ventricular tachyarrhythmias which have not responded to medical therapy may recur at any time. The insertion of AICD patches at the time of myocardial revascularisation surgery will prolong the procedure. In order to obtain satisfactory patch placement repeated testing of defibrillator thresholds in response to induced VF may be necessary. These can produce a temporary reduction in ejection fraction that requires the interruption of testing and increases the probability of the patient requiring inotropic support to be taken off cardiac bypass successfully.

The anaesthetic considerations for insertion of AICD, leads and patches, without coronary grafting, are the same as for any major cardiac procedure. Full monitoring, including intra-arterial pressure and central venous or pulmonary artery pressure, is mandatory. This applies to implantation of the AICD device alone, when leads and patches are already *in situ*. Induction of VT/VF to test defibrillator function and thresholds will occur at the initial insertion and again under general anaesthesia about 3 months later.

The peri-operative mortality associated with AICD implantation is 0–8% in different series,[2,6-8] depending on the extent of surgery undertaken and the pre-operative condition of the patient. A more recent series showed a 30-day mortality of 5.6% for all AICD procedures and 10.7% for AICD implant plus coronary artery bypass grafting.[13] There is also significant morbidity associated with the procedure. Wound infections occur in 2–20%[5-9] and large pleural effusions in 4–10%, depending on whether the device is implanted into the abdomen or thorax.[5,6] Asymptomatic shocks occur in 8–45%[5,6,10] and the re-operation rate 3.8–14%.[6,9,11]

At postoperative testing of the AICD, an 8% incidence of failure to revert the ventricular tachyarrhythmia has been reported.[2,6] Testing is usually performed on one occasion with the patient conscious, so that the mild discomfort of the AICD shock can be experienced. If the device fails and external defibrillation is required, an anaesthetist may be called urgently.

As the number of patients receiving these implants increases, some of them will inevitably require anaesthesia for noncardiac surgical procedures. In the case of elective surgery, the cardiology department should be contacted in advance so that the functioning of the AICD can be assessed, its frequency of firing ascertained and the attendance of trained personnel during surgery guaranteed. The presence of an external defibrillator and full resuscitation equipment is mandatory for any procedure involving these patients. If surgical diathermy is considered essential, bipolar electrodes should be used. However, during periods of diathermy, close monitoring of cardiovascular and AICD function is essential. The device may be disabled by holding a magnet over it, but it should be emphasised that experience with the AICD during noncardiac procedures is limited, therefore expert assistance must be available to ensure the safety of both the patient and the AICD.

Special precautions are required, in particular for electroconvulsive therapy (ECT).[14] The AICD needs to be disabled before induction of anaesthesia. Earthing of the patient must be avoided to prevent VF being triggered by the ECT current passing through the heart via the AICD.

Acknowledgments

Figures 1 and 2 are reproduced, with kind permission, from the Telectronics Guardian 4202 Clinical Application Manual.

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Anaesthesia, 1991, Volume 46, pages 741–743

CASE REPORT

Removal of a laryngeal foreign body using high frequency jet ventilation

S. S. TAN, S. S. DHARA AND C. K. SIM

Summary

Aspiration of a foreign body into the respiratory tract is a common and serious accident in childhood. Laryngotracheal foreign bodies, although less common than bronchial foreign bodies, are potentially more dangerous. Removal is commonly achieved using a rigid ventilating bronchoscope. We report a 16-month-old boy who had an open safety pin impacted in his larynx. This was removed through a tracheostomy, using high frequency jet ventilation to maintain gaseous exchange. We believe that this is the first case in which this method of removal has been reported.

Key words

Larynx; foreign body.
Ventilation; high frequency.

Case history

A 16-month-old child weighing 10 kg was admitted with a 2-week history of hoarseness, sore throat, dysphagia and noisy breathing during sleep. He had been treated by three general practitioners, the last of whom noted that the child was cyanosed and sent him to the Accident and Emergency Department. On admission, the child was pink, but on crying, had a tinge of cyanosis. He had obvious inspiratory stridor and throat noises as a result of secretions, but on auscultation his lungs were clear. An anteroposterior X ray of the neck showed an open safety pin lodged in the midline in the upper part of the neck. The child was distressed by the procedure therefore no lateral films were taken. Direct questioning of the mother revealed that, 2 weeks before, the child was playing with a safety pin while she was sewing.

After reviewing the child in the ward, the anaesthetist applied EMLA cream to the dorsum of both hands and the child was brought to the operating theatre in his mother's arms. No premedication was given. An electrocardiograph (ECG) and pulse oximeter were applied before induction and equipment was available for emergency cricothyrotomy (16-G Vasocan, Braun) and tracheostomy. The surgeon was in the operating theatre and ready to proceed immediately, if necessary. Anaesthesia was induced and maintained with 100% oxygen and halothane without difficulty. A careful laryngoscopy revealed that the pointed end of the open safety pin was below the vocal cords. The buckle of the pin was above the vocal cords and hooked over the posterior rim of the laryngeal aperture (Figs 1 and 2). It was immediately apparent that it would not be possible to withdraw the pin without lacerating the trachea and vocal cords. There was an additional problem of maintaining adequate depth of anaesthesia during laryngoscopy and there was a tendency for the child to develop laryngospasm under light anaesthesia. As the airway was easily maintained, a decision was then made to administer neuromuscular blockers and proceed with a tracheostomy. Atropine 0.1 mg and suxamethonium 12.5 mg was given. Artificial ventilation was easily maintained with a bag and mask whilst a tracheostomy was performed through a transverse skin incision. The cervical trachea was exposed by separating the strap muscles longitudinally. Two 3–0 polypropylene stay sutures were then placed on the trachea so that traction on them would both stabilise the trachea and keep the tracheostomy open. A vertical incision was made in the trachea, between these stay sutures, over the third and fourth tracheal rings. A size 4 noncuffed Portex tracheostomy tube was inserted. Anaesthesia was continued with nitrous oxide 3 litres/minute and oxygen 1.5 litres/minute via a modified Ayre's T-piece. The tracheostomy tube was then replaced by a size 10 suction catheter, cut to 15 cm and attached to a size 2.5 Portex connector. Approximately 2 cm of catheter was inserted so that the tip

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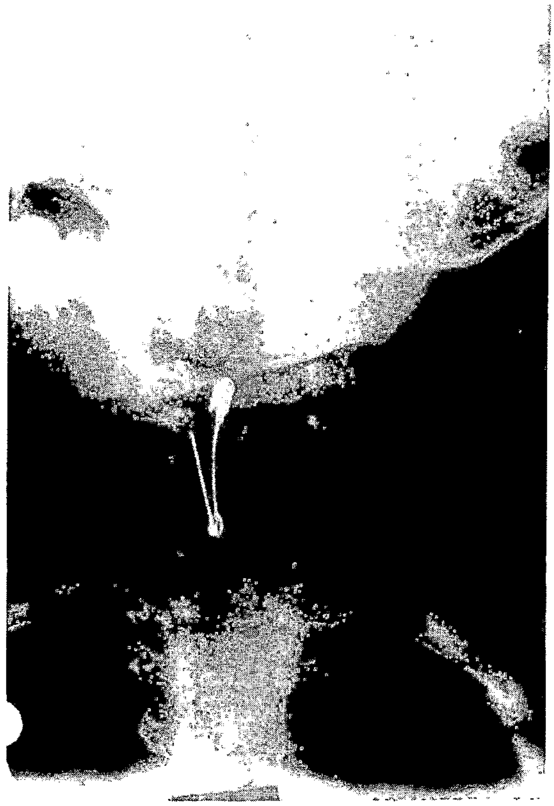

Fig. 1. Antero-posterior X ray of neck showing safety pin.

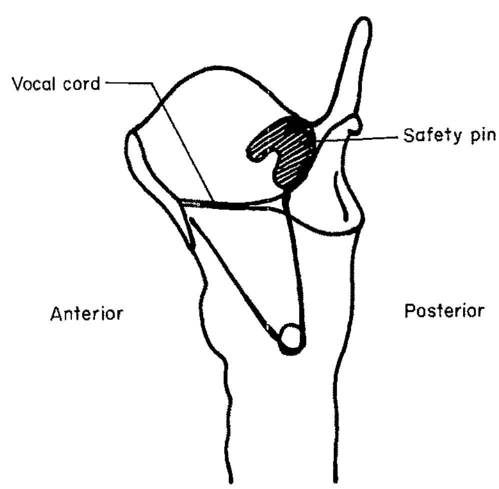

Fig. 2. Cross-section of larynx showing position of safety pin.

was positioned just above the carina. Accidental decannulation was prevented by fixing the tube with a single suture going through the skin, platysma and deep cervical fascia. A rigid bronchoscope was inserted into the tracheostome towards the larynx until the bottom of the safety pin was seen. Direct laryngoscopy was then performed from above and the buckle of the safety pin was grasped and advanced into the trachea just distal to the vocal cords. The safety pin was finally removed through the tracheostomy using the rigid bronchoscope. Anaesthesia was maintained with diazepam (a total of 2 mg over 40 minutes). Increments of atracurium provided neuromuscular blockade and high frequency ventilation with approximately 40% oxygen in air was applied. The ventilator used works on the principle of pneumatic logic (Percussionaire[R] Corporation, Sandpoint, Idaho 83864, USA, model TXP). A variable amount of air is entrained, depending on the compliance of the patient's lungs; the oxygen percentage ranges from 40% in normal lungs to 100% in non-compliant lungs. Haemoglobin oxygen saturation remained at 98–100% during the 2-hour procedure. After removal of the safety pin, a repeat laryngoscopy showed marked oedema of the oropharynx and areas of ulceration on the vocal cords. The suction catheter was finally replaced with a size 4 tracheostomy tube and neuromuscular blockade was reversed with neostigmine 0.5 mg and atropine 0.2 mg. When spontaneous respiration was adequate, the patient was transferred to the Intensive Care Unit for observation.

Examination under anaesthesia 24 days later showed that the larynx had healed without scarring. The tracheostome was decannulated 3 days later and the patient was discharged on the 30th day. A review 2 weeks later showed that the child was well and he was discharged from further follow-up.

Discussion

Aspiration of a foreign body into the respiratory tract is a common accident, which occasionally has a fatal outcome. It is said to be one of the commonest recognised causes of sudden death, especially in children.[1] The majority of inhaled foreign bodies are lodged in the bronchial tree; in five series of cases an incidence of 88–96% was reported.[2–6] Our patient was 16 months old; in four series the commonest age group was 1–3 years and this group accounted for 48–80% of patients.[4,6–8]

The larynx is a much less common site and accounted for only 2–6.7% of cases.[2–4,6] Our patient presented with hoarseness and stridor, features which suggested that the larynx was involved rather than the lower respiratory tract; dyspnoea, cough and stridor are reported to be the commonest symptoms and signs of laryngotracheal foreign bodies.[4] Although a history of a choking episode is obtained in the majority of patients with inhaled foreign bodies (73–85%),[2,4,5] the diagnosis may be delayed. In one study, the length of time to diagnosis ranged from less than 24 hours in 55% patients to 5.5 months in 5% of cases. However, most laryngotracheal foreign bodies were diagnosed within a week, probably because of the greater severity of symptoms.[7] This is in contrast to bronchial foreign bodies, the diagnosis of which may be delayed.

A strong index of suspicion, specific questioning and careful examination of X rays of the neck and chest (posterior–anterior and lateral), should aid diagnosis. Signs of upper airway obstruction, such as stridor, positional dyspnoea, cyanosis and wheezing, should be sought. A detailed pre-operative assessment is essential, since the anaesthetic, like the operative technique, is determined by the site of the foreign body and any secondary complications.

The management of laryngotracheal foreign bodies is a team effort which involves a skilled and experienced endoscopist and assistant, equally skilled and experienced anaesthetists, and a scrub nurse. The whole procedure should be well planned, with careful monitoring of the patient's pulse, blood pressure, ECG and oxygen saturation. Intravenous access is essential.

In this case, we would like to emphasise two important surgical details. The stay sutures on the trachea should be inserted before opening the stoma. This allows the assistant

to stabilise the trachea during change of tube and instrumentation. It is important to fix the catheter used for high frequency ventilation, to prevent decannulation during instrumentation. The catheter should be sutured to the deep cervical fascia, which is closely adherent to the trachea, and not just to the skin, which is freely movable. The safety pin could only be removed in one direction, therefore it was important to advance it just distal to the vocal cords, yet not allow it to slip beyond the tracheostomy into the intrathoracic portion of the trachea.

The commonest method of removal of a foreign body is through a rigid bronchoscope in a spontaneously breathing patient.[6,7–9] Flexible fibreoptic bronchoscopy is less commonly reported[10,11] and indications for its use are not as well defined.

Simultaneous bronchoscopy and tracheostomy with removal of the foreign body through the tracheostomy has been described,[12] but we believe that this is the first reported case in which the technique of high frequency jet ventilation through the tracheostome was used during removal of the foreign body.

Complications after bronchoscopy are uncommon, but can include laryngospasm and laryngeal oedema. Laryngospasm may be prevented by adequate topical analgesia of the larynx and intravenous dexamethasone may help to reduce airway oedema.

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Anaesthesia, 1991, Volume 46, pages 744–746

CASE REPORT

Extracorporeal circulation in the management of massive propanolol overdose

F. K. MCVEY AND C. F. CORKE

Summary

A case of refractory hypotension following propanolol overdose is reported. Management included isoprenaline, glucagon and extracorporeal circulatory support using femoral vein–femoral artery bypass. The unreliability of neurological observations, especially unreactive pupils, in the presence of drug overdose is reiterated.

Key words

Sympathetic nervous system, β-adrenergic antagonists; propanolol.
Complications.

Case history

A 20-year-old woman was admitted to the Accident and Emergency Department having ingested approximately 50 of her mother's propanolol tablets (total 2 gm) and 10 Mersyndol tablets (paracetamol 45 mg, codeine 9.7 mg, doxylamine 5 mg). Three hours before admission, her mother reported that she was well. However, in the hour before admission, the daughter told friends of her action and they induced her to vomit. Some tablets were seen in the vomitus. After half an hour, she became drowsy and an ambulance was called. The ambulance crew found her unresponsive, with focal fitting, dilated but sluggishly reacting pupils, no recordable blood pressure and a slow capillary refill time, but she was breathing spontaneously. She was given oxygen by mask and transferred in the lateral decubitus position.

Her past medical history included mild asthma as a child. She had no psychiatric history. She lived with her mother and had a 2-year-old child. Recent relationship problems with her boyfriend had precipitated her overdose.

She was unrousable on admission, intermittently fitting and peripherally cyanosed. No pulses were palpable and blood pressure was unrecordable. The ECG showed a broad QRS complex and bradycardia of 40 beats per minute. Blood gases during resuscitation were pH 6.96, $Pa\text{CO}_2$ 4.72 kPa, $Pa\text{O}_2$ 73.0 kPa, base deficit 20.7. Urea and electrolytes were normal. Blood glucose was 6.5 mmol/litre. Paracetamol level was 33 mmol/litre; no tricyclics were detected. Subsequently propanolol levels were found to be greater than 4589 ng/ml.

She was initially oxygenated by mask ventilation, followed by tracheal intubation and ventilation with 100% oxygen. External cardiac massage was initiated and continued throughout her subsequent resuscitation (total of 4 hours). Gastric lavage was performed, but no tablets were recovered. Activated charcoal was instilled into the stomach. Clonazepam 1 mg was given to relieve seizure activity and atropine 1.2 mg was administered for bradycardia. During the first hour, she received two boluses of isoprenaline 200 μg followed by an infusion of 20 μg per minute and two boluses of adrenaline 1 mg, followed by an infusion of 25 μg per minute. She also received 2 litres of intravenous colloid. There was no improvement in her pulse or blood pressure, and her central venous pressure was 35 cmH_2O. Glucagon was given as it became available, to a total of 9 mg over 90 minutes. Her carotid pulse became intermittently faintly palpable following glucagon administration. Her ECG continued to show a bizarre broad complex bradycardia of 30 to 40 beats per minute. Transvenous cardiac pacing was unsuccessful because of a complete failure to capture and no improvement in cardiac output. During this time a further 6 mg of glucagon was located and administered, and subsequently radiographic screening revealed some slight cardiac movement.

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Although her pupils remained dilated and unresponsive, she was seen to flex her arms spontaneously to intensely painful stimuli. It was decided to try mechanical haemodynamic support using femoral-femoral extracorporeal circulation.

Bard 20 French gauge multiple hole 'CPS' cannulae were inserted into the right femoral vessels using a cut-down technique. After systemic heparinisation, extracorporeal circulation was established using a Biomedicus centrifugal pump and a Cobe CML membrane oxygenator. This achieved an initial blood flow of 3.5 litres/minute. A Gambro 'Absorber' charcoal haemoperfusion filter was added to the system with a flow of 200 ml/minute. External cardiac massage was discontinued following the successful institution of extracorporeal circulatory support. Intermittent positive pressure ventilation was continued to maintain mild hypocapnoea. There was progressive improvement in her haemodynamic status, and inotropic support was gradually withdrawn. At 10 hours after admission, her pulse was 76/minute and blood pressure 120/80 mmHg. The patient was weaned from the extracorporeal support and the femoral catheters removed. At this time, her pupils were briskly reactive, she responded appropriately to command and moved all four limbs. Spontaneous ventilation was adequate and her trachea was extubated. Urine output was good. Propanolol levels were greater than 948 ng/ml after weaning from all haemodynamic support. During the following day, she achieved a full neurological and cardiovascular recovery. She was referred for psychiatric assessment and care.

Discussion

There are now several reports of propanolol overdose in the literature.[1-10] This report illustrates the presentation, therapeutic options and management problems presented by severe propanolol toxicity, and suggests that extracorporeal support of the circulation may successfully supplement pharmacological treatment.

The features of propanolol intoxication are primarily cardiovascular, with bradycardia occurring in 90% and hypotension in 77%.[10] Membrane stabilisation occurs at plasma levels 50 to 100 times those required for beta-adrenoceptor blockade, resulting in heart block and widening of the QRS complex. Other beta-adrenergic blocking agents without membrane stabilising activity, and those possessing intrinsic sympathomimetic activity frequently cause only mild haemodynamic disturbance in overdose.[5,10] Propanolol is also highly lipid soluble and readily crosses into the central nervous system. Seizures have been described in 58% of cases of overdose, caused by a combination of hypoxia and membrane stabilisation, comparable to lignocaine toxicity.[3,5,6,8-9,10]

The symptoms of overdose occur 1 to 2 hours after ingestion, coincident with peak plasma levels. Sudden collapse often occurs in association with induced vomiting or intubation, and is attributed to intense and unopposed vagal stimulation.[4,7,9,10] The severity of the overdose is better reflected by clinical findings than plasma levels.[10] One patient has survived ingestion of 8 g of propanolol,[3] while fatalities have occurred with much smaller doses.[4] Emergency treatment consists of basic life support, gastric lavage and instillation of activated charcoal. Atropine given before intubation or gastric lavage may prevent sudden deterioration due to vagal stimulation, but during resuscitation, is usually ineffective.[10] Volume expansion in our patient was poorly tolerated and failed to improve the haemodynamic status.

Conventional inotropes, including adrenaline and dopamine, are frequently ineffective in severe propanolol toxicity.[3,5,8,10] Isoprenaline, although the logical choice, is rarely beneficial except in 'mild' toxicity.[3,5,7,8,10] although very high dose isoprenaline (200 μg/minute) was successful in one case.[11] Glucagon has consistently been reported to have a beneficial effect on heart rate and blood pressure in beta-blocker overdose.[1,2,5,9,10] In pharmacological doses, it has both inotropic and chronotropic effects.[12] Chronotropism is partially beta-receptor mediated and is reduced by beta-adrenergic blockade. However, inotropism is mediated by activation of adenyl cyclase at a site different from the beta-adrenergic receptor (resulting in increased intracellular cyclic AMP) and increased intracellular calcium flux, but there is no increase in myocardial irritability.[12] The recommended dose of glucagon in this situation is 50 to 150 μg/kg bolus, followed by an infusion of 1 to 5 mg/hour.[10] The effect occurs at 5 minutes and lasts for 30 minutes. Side effects include nausea and mild hypoglycaemia.[12] Glucagon potentiates the anticoagulant effects of warfarin but not heparin,[12] which was an important consideration in the institution of an extracorporeal circulation. The problems associated with the use of glucagon include difficulty locating adequate supplies.[1,2,4] Our entire hospital stock was 18 mg distributed between casualty, the Intensive Care Unit, the radiology and paediatric departments. One previous case of failure of glucagon to improve the haemodynamic status in propanolol overdose has been reported.[3] The authors attributed this to the inability of glucagon to reverse the membrane stabilisation effect. Our patient had a poor response to glucagon, had signs of membrane stabilisation with pronounced heart block and bizarre broad QRS complexes.

Mechanical methods of haemodynamic support include transvenous pacing which resulted in increased heart rate but not blood pressure in four out of five reported cases.[6,10] In one case repeated failure to capture was reported, as in our case above. Intra-aortic balloon counterpulsation has been successfully used to augment cardiac output when pharmacological methods, including glucagon, had failed.[3] In our case, however, the lack of any significant intrinsic cardiac output suggested that intra-aortic balloon counterpulsation was unlikely to be of benefit. Extracorporeal circulatory support has not previously been described in the management of severe beta-blocker toxicity. The use of large percutaneous femoral cannulae permitted rapid placement and adequate flows to maintain the circulation. The addition of a charcoal haemoperfusion column may have helped to shorten the duration of toxicity. However, propanolol is 90% to 96% protein bound and removal by charcoal haemoperfusion is low.[13]

Several other cases have been reported of complete neurological recovery after cardiac arrest and seizure activity induced by propanolol overdose. It has been suggested that propanolol may have a cerebral protective effect.[3,10] Propanolol crosses the blood-brain barrier easily achieving high CNS levels (10 to 20 times plasma levels).[14] Coma is more likely to be due to propanolol itself, rather than hypoxia or ischaemia in most cases of overdose. Neurological signs such as pupil reactivity and size are

unreliable indications during resuscitation particularly in the context of drug overdose. We reiterate the statement by Safar and Bircher:[15] 'It is impossible to judge the salvageability of the brain during emergency resuscitation... termination of emergency efforts is justified only when there is solid evidence of irreversible cardiac arrest'. With reference to beta-blocker overdose Wernstein states[10] 'If the patient arrives alive, experience predicts a good prognosis with appropriate therapy'. Our patient had dilated unreactive pupils for 6 hours from the time of admission. Her complete recovery reinforces the above statements.

Acknowledgments

We are indebted to Dr P. Phillips for permitting us to report this case who was under his care.

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Anaesthesia, 1991, Volume 46, pages 747–749

CASE REPORT

Possible inadvertent subdural block following attempted stellate ganglion blockade

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Summary

A case is reported of suspected inadvertent subdural block following attempted stellate ganglion blockade for relief of cervicobrachial pain in a patient suffering from reflex sympathetic dystrophy. Possible complications due to neuraxial spread of local anaesthetics while performing a cervicothoracic ganglion blockade are considered.

Key words

Anaesthetic techniques, regional; stellate ganglion block.
Complications.

Blockade of the stellate ganglion has been used for a wide variety of conditions. It is known to produce excellent relief from chronic pain in reflex sympathetic dystrophy (RSD), a pain syndrome mediated by sympathetic pathways.[1] Moore described 16 possible approaches to the stellate ganglion[2] but the anterior paratracheal approach at the C_6 level, described by Lofstrom[3] and Carron and Litwiller[4] is most commonly used because it has the advantage of placing the needle well above the dome of the pleura and anterior to the plane of the roots of the brachial plexus. However, in spite of taking all precautions complications are possible, even in experienced hands.

This report describes a high central neural block, with loss of consciousness, following an attempt to block the stellate ganglion. The most probable cause was an inadvertent injection of local anaesthetic solution into the subdural extra-arachnoid space.

Case history

A 38-year-old woman suffering from causalgia in the right arm was a frequent attender at the Pain Clinic. She obtained fairly good pain relief with spinal cord stimulation, but once or twice each year a more severe burning pain, originating from the affected area, necessitated additional therapy. Previous similar painful episodes had been treated with a stellate ganglion block using plain bupivacaine 0.5% which provided excellent analgesia lasting several months.

The patient attended the Pain Clinic with another exacerbation and was scheduled for a stellate ganglion block. Standard routine monitoring precautions were taken: an intravenous gelatine solution was started, the heart rate was monitored by electrocardiogram (ECG) and arterial blood pressure was noninvasively measured at 5-minute intervals. The patient was placed in the supine position and the block performed using the anterior paratracheal approach at the C_6 level. A 22-gauge needle was inserted perpendicularly to the skin and bony contact was made. Withdrawal of the needle by 1–2 mm and aspiration revealed no blood or cerebrospinal fluid (CSF).

An initial dose of 2 ml of plain bupivacaine 0.5% was injected. The patient reported a sensation of pressure, localised in the neck at the level at which the block was being performed. The aspiration test was repeated and again no signs of possible misplacement of the needle were detected. The infiltration was then completed, with a total dose of 10 ml of plain bupivacaine 0.5%, and the patient was placed in a 45° sitting position.

Approximately 1 to 2 minutes after completion of the injection, the patient reported a tingling sensation in both arms and hands and complained of a nauseous feeling. A few seconds later she lost consciousness and stopped breathing. Cardiovascular variables at that moment showed no changes: heart rate remained at about 80/minute and the blood pressure was 120/70 mmHg.

Standard resuscitation measures were immediately started with placement of the patient in the supine position,

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tracheal intubation and positive pressure ventilation of the lungs. Examination of the pupils showed them to be intermediately dilated with no reaction to light. After 30 minutes, during which no haemodynamic or neurological changes occurred, the patient was transferred to the intensive care unit (ICU) for continued monitoring and ventilation.

One hour after the injection the only reaction to pain was a slight movement of the eyelids, with no change in the cardiovascular parameters and nonreactive dilated pupils. After 2.25 hours, the patient slowly regained consciousness, with increasing heart rate and blood pressure upon stimulation. The pupil size returned to normal but remained unreactive to light. After 2.75 hours, the patient was fully conscious, respiration was adequate and her trachea was extubated. Motor function of the upper and lower limbs showed no paralysis but the patient reported that her legs felt 'anaesthetised'. The patient was discharged from the ICU on the following day with no permanent sequelae. The initial pain condition was relieved and, as was discovered later, the pain relief lasted for a prolonged period.

Discussion

The clinical signs of apnoea and loss of consciousness led us to an initial diagnosis of an intrathecal injection resulting in a total spinal block, in spite of the fact that all reasonable precautions had been taken. Needle placement had been performed exactly according to that described for the anterior paratracheal approach and an aspiration test repeatedly showed no sign of CSF. However, failure to obtain CSF on aspiration does not preclude the possibility of an intrathecal injection.

There are only three ways that the local anaesthetic could have entered the intrathecal space.[5] Firstly, improper needle advancement, directed intrathecally through the intervertebral foramen, seems improbable in view of the paratracheal approach chosen. Bony contact was made as expected, with the needle never being directed in a medial direction. Secondly, a dural cuff may accompany a nerve root some distance distal to the intervertebral foramen. Cadaver studies have demonstrated dural cuffs extending as far as 8 cm laterally, making direct intrathecal injection possible, no matter which approach to the stellate ganglion is chosen. Thirdly, local anaesthetics injected perineurally can diffuse back into the subarachnoid space. However, this mechanism has a relatively long onset time and requires a large dose to become clinically important.

After reconsidering the sequence of symptoms and signs in this case, we considered that our initial assumption of a total spinal block might not be the correct diagnosis, since the clinical picture seemed incomplete without bradycardia and marked hypotension.[6–8] This will certainly occur if the subarachnoidally administered dose is large enough to produce unconsciousness and dilated pupils, as a concomitant widespread sympathetic blockade will result in marked hypotension.[9] Cases of inadvertent total spinal blockade are reported as accompanied by severe arterial hypotension and occasionally by life threatening cardiac rhythm disturbances.[10–12]

Moore has reported cases of high epidural block following stellate ganglion blocks with 10 ml of local anaesthetic. In these cases onset was more gradual and the resulting block only involved the upper extremities with no loss of consciousness, since the epidural space does not extend intracranially.[13]

Subdural extra-arachnoid injections of local anaesthetic solutions have been described; most of them occurred inadvertently while performing epidural blocks. The subdural space is a potential cavity between the dura mater and the arachnoid mater, containing a small quantity of serous fluid, but no CSF. It does not communicate directly with the subarachnoid space but extends laterally over the nerve roots and ganglia with a cephalad extension intracranially. The subdural space is wider in the cervical region than elsewhere and also adjacent to the nerve roots.[14] Onset of blockade has been described as both fast and slow.[15,16] In all of these cases an unexpectedly high level of sensory block was described, with loss of consciousness lasting from one to several hours. As in our case a remarkable stability of cardiovascular parameters was observed, a phenomenon for which no good explanation has been proposed. The selective dorsal distribution of the local anaesthetic solution, a slow rate of spread or a mainly unilateral ascent of the analgesic mixture are hypotheses advanced but still to be proven.[17]

We think that the loss of consciousness and the accompanying symptoms in our patient were caused by an injection of local anaesthetic into the subdural space, most probably in a dural cuff extending laterally along a nerve root at the C_6 level.

The occurrence of an extensive subdural extra-arachnoid block has the potential of causing severe complications such as total subarachnoid block, from which, in the acute phase, it can be differentiated only with difficulty. It is even more difficult to prevent as an aspiration test will not reveal any CSF.

Our patient made a full recovery from this complicated attempt at stellate ganglion blockade, with no sequelae and with good pain relief that lasted as long as after previous uncomplicated blocks. Subdural blocks performed under radiographic control and using minute quantities of local anaesthetic have been proposed as an effective method to relieve pain in patients suffering from inoperable neoplasms in the cervical region.[18]

Finally, we must stress that no form of regional blockade should be undertaken unless means of monitoring and supporting the respiratory and cardiovascular systems are readily available and functioning.

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APPARATUS

An assessment of the Cerebrotrac 2500 for continuous monitoring of cerebral function in the intensive care unit

E. S. SHEARER, E. P. O'SULLIVAN AND J. M. HUNTER

Summary

Experience of the use of the Cerebrotrac 2500 EEG monitor in 17 patients subjected to artificial ventilation in an intensive care unit is reported; seven were receiving continuous sedation with morphine, midazolam and propofol singly or in combination and 10 received both sedation and the neuromuscular blocking agent, atracurium. The processed EEG patterns could not be precisely correlated with a standard clinical scoring system but were useful in determining the adequacy of sedation, particularly when a muscle relaxant was used. The monitor also shows considerable promise in the management of the paralysed patient with widespread convulsive activity in whom ischaemic brain damage may be occurring from epileptiform activity in the absence of any clinical manifestation. The ability to detect cerebral irritability or isolated epileptiform discharges using this apparatus is, however, questionable. The equipment was easy to use and robust; the running costs were 9.5p per hour.

Key words

Equipment; Cerebrotrac 2500.
Monitoring; cerebral function.

The original techniques for processing electroencephalographic (EEG) data into a form easily interpreted by the inexperienced had several disadvantages. The cerebral function monitor (CFM) gave only a gross indication of global cerebral activity,[1] whilst the output format of its successor, the cerebral function analysing monitor (CFAM),[2] was found by many to be difficult to interpret. To overcome this problem attention has been directed to new forms of data presentation. The first development was the compressed spectral array (CSA).[3] This displayed EEG activity in the frequency domain as three-dimensional peaks and troughs, which unfortunately led to a loss of data since large peaks could cause previously recorded activity to be obscured. Two recent additions in this field, density spectral array (DSA)[4] and spectral edge frequency (SEF),[5] appear to offer considerable promise because the style of data output is relatively easy to interpret and the hardware required inexpensive.[6] Both these are used in the Cerebrotrac 2500.

Although the use of cerebral function monitoring during surgery has received considerable attention,[2,7,8] there is little information regarding its use over prolonged periods on the intensive care unit (ICU). We therefore decided to assess depth of sedation and cerebral function in critically ill patients in an ICU receiving continuous infusions of sedatives, analgesics and in some cases the neuromuscular blocking drug, atracurium, using a Cerebrotrac 2500 monitor (Neurosciences Ltd). This report describes our experience with the monitor and discusses the usefulness of this form of EEG recording in ICU patients.

Materials

Equipment

The monitor is a dual channel bipolar device which utilises fast Fourier transform (FFT)[9] to convert EEG waveforms from the time domain to the frequency domain; a procedure known as Real Time Spectral Analysis (RTSA). In order to perform FFT on the incoming signal, the microprocessor first divides the signal into discrete time periods (epochs). The Cerebrotrac 2500 uses an epoch of 2 seconds. All information in that epoch (frequency and amplitude) is then processed and the resulting data presented in enhanced colour on the video display unit. For display purposes the frequency data uses a DSA format. With this technique, each epoch of the spectral analysis is displayed as a line of varying density. The areas of maximum intensity correspond to those frequencies making the largest contributions to the EEG spectrum. The total EEG ampli-

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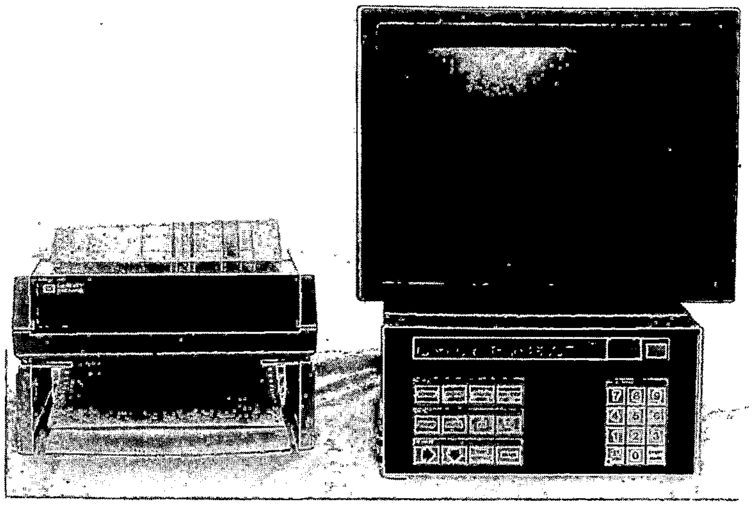

Fig. 1. The Cerebrotrac 2500 screen and controls are shown, together with the hard copy jet printer.

tude (calculated from the spectra generated by RTSA) is displayed in both digital and trended format. A solid line overlaid on the DSA represents the SEF, which is the highest frequency at which a significant amount of energy is present in the EEG during that epoch and which acts as an indicator of the overall trend of EEG activity. In addition to the frequency, amplitude and SEF display, the monitor also allows direct visualisation of the unprocessed real time EEG data (Fig. 1).

All of the processed data can either be downloaded via an RS–232 interface to a computer data base or, as in this study, stored in hard copy form using an ink jet printer. A further option, available at extra cost, allows the user to obtain a 'snapshot' hard copy printout of either 8 or 24 seconds of unprocessed EEG signal.

Complementary to the EEG monitoring, there is a continuous graphical display of the electromyograph (EMG) of the frontalis muscle, thus allowing the identification of possible muscle tone artifacts. The monitor can be interfaced with up to four other patient monitors at any one time, e.g. heart rate, blood pressure, temperature. These variables can then be displayed continuously alongside the processed EEG. The cost of the equipment (including ink jet printer and 'snapshot' option) when purchased in August 1989 was £8500 (VAT exempt).

The monitor records the EEG signal via five 9 mm silver/silver chloride disc electrodes fixed to the scalp with colloidon and filled with conductive electrode jelly. In order to ensure high quality recording, the impedance of the electrodes must be maintained at less than 20 Kohms, preferably less than 5 Kohms. The monitor incorporates a facility which allows the electrode impedance to be checked without interrupting data collection. We attached the five EEG electrodes at the F3/P3 and F4/P4 positions (as described in the International 10/20 system),[10] with the ground lead positioned over the midfrontal region. These electrode sitings were chosen since they cover a wide area of cerebral cortex including the main arterial boundary zones, whilst avoiding sources of unwanted signals such as eye or jaw movement.[11] After use, all the electrodes were cleaned, rechlorided overnight in domestic bleach and re-used.

Methods

Seventeen patients whose lungs were being artificially ventilated were monitored for part of their stay on the ICU. Patients were divided according to clinical indication into two groups: group 1 consists of seven patients who were receiving sedation with a combination of either morphine, midazolam or propofol and group 2 of 10 patients who were receiving a constant infusion of atracurium, in addition to sedation. Informed consent was obtained from the next of kin before the start of monitoring. The clinical level of sedation was regularly assessed throughout the monitoring period using a five-point scale modified from that described by Shelly and colleagues.[12] Thus, with Shelly score 1, the patient is awake and alert; with score 2, asleep but roused by voice; score 3, asleep, roused only by pain; score 4, unrousable; and score 5, receiving neuromuscular blocking agents.

We attempted to determine the usefulness of the Cerebrotrac 2500 as an ICU monitor with respect to reliability,'user friendliness' and cost; the correlation between the EEG changes and the level of sedation as assessed clinically; the detection of potential convulsive activity.

Results

Reliability, 'user friendliness' and cost

The layout of the control panel of the Cerebrotrac 2500 is simple with the minimum of controls, many of which have a dual function (Fig. 1). The prominence of the on/off button may, however, lead to the monitor being switched off inadvertently and this problem needs addressing. The 'start-up' procedure was self-explanatory and alteration of the monitor configuration was easy. At no time did we encounter any failure of the monitor and found both the monitor and the printer entirely reliable.

The main practical problem lay with the difficulty in maintaining good electrical contact with the scalp for prolonged periods. The attachment of the silver electrodes can prove difficult. Initially we sought the assistance of EEG technicians but with further experience the authors took on the task themselves. Correct electrode placement

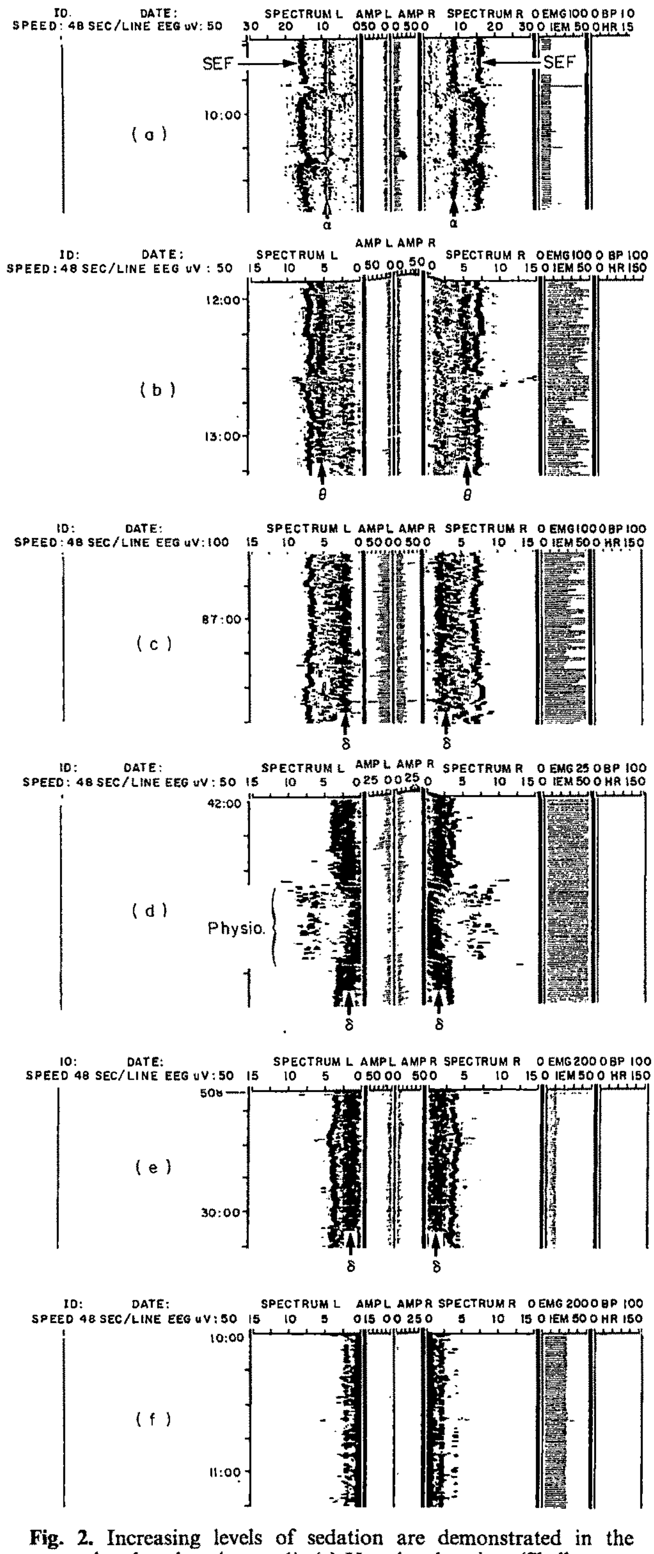

Fig. 2. Increasing levels of sedation are demonstrated in the unparalysed patient (group 1). (a) Unsedated patient (Shelly score 1) with dominant alpha (α) wave activity and a SEF of approximately 15 Hz. (b) With the institution of sedation, the α wave disappears and is replaced by a dominant theta (θ) wave and a fall in the SEF to 7 Hz: this patient had a Shelly score between 1 and 2. (NB) there is a change in the frequency scale between traces (a) and (b)). (c) As sedation is further increased, low frequency delta (δ) activity appears, of high amplitude, equivalent clinically to a Shelly score of 2. (d) When the patient is satisfactorily sedated, albeit aroused by pain (Shelly score 3) a dominant delta wave is present with a low SEF (less than 5 Hz) but the activity is increased by the stimulation of physiotherapy. (NB, there is a change in the amplitude scale between Fig. 2(c) and 2(d).) (e) An unresponsive patient (Shelly score 4) with a recording consisting almost entirely of delta activity. (f) In the presence of excessive sedation, electrical activity is barely visible on the tracing (also Shelly score 4). The electromyograph of the frontalis muscle is visible on the right hand side of each recording.

Table 1. The cost of consumables for the Cerebrotrac 2500 during the 7-month study period.

Item	Cost £
Ink jet cartridges	128.00
Replacement electrodes	93.00
2 cc disposable syringes	56.00
Ink jet paper	36.00
Disposable blunted needles	29.00
Colloidon	14.00
Electrode jelly	6.00
Total	£362.00

took up to one hour but once attached was extremely robust. On average the electrodes only required to be resited every 10 days. This was invariably the result of dislodgement during general nursing care. Three weeks was the longest period a single set of electrodes were attached. At no time did we encounter any problems such as skin irritation or ulceration from prolonged contact. However, the conductive jelly dried up frequently leading to an increase in impedance and subsequent loss of signal quality. The impedance was checked on the control panel several times a day and fresh jelly applied as required. Nevertheless we found that the signal was lost because of poor electrical contact for an average of 19% of the total monitoring time; this loss was always at night if one of the authors was not available.

The consumables required to operate the monitor over the 7-month study period together with the total cost incurred during that period, are listed in Table 1. The overall cost of using the monitor for the 7-month study period was 9.5p per hour.

Level of sedation

We used the Cerebrotrac for a total of 3781 hours of patient monitoring: the average duration was 222 hours; the single longest run was 885 hours. In neither group was it possible to correlate specific EEG patterns with particular sedative drugs. It was found, however, that by comparing the level of sedation as assessed clinically with the output of the Cerebrotrac 2500, it was possible to identify specific EEG patterns in group 1 patients which were associated with a particular depth of sedation, although these degrees did not correspond exactly with the Shelly sedation score (Fig. 2).

In group 2 patients the EEG pattern of a deeply sedated patient was invariably found, with traces very similar to that shown in Figs 2(e) and 2(f) (equivalent to a sedation score of 4). At no time did we see an EEG trace in a paralysed patient which we considered could have been compatible with only light levels of sedation (sedation score 1–2).

Convulsive activity

Two patients in group 2 developed epileptiform activity during the study period. One patient, who was receiving

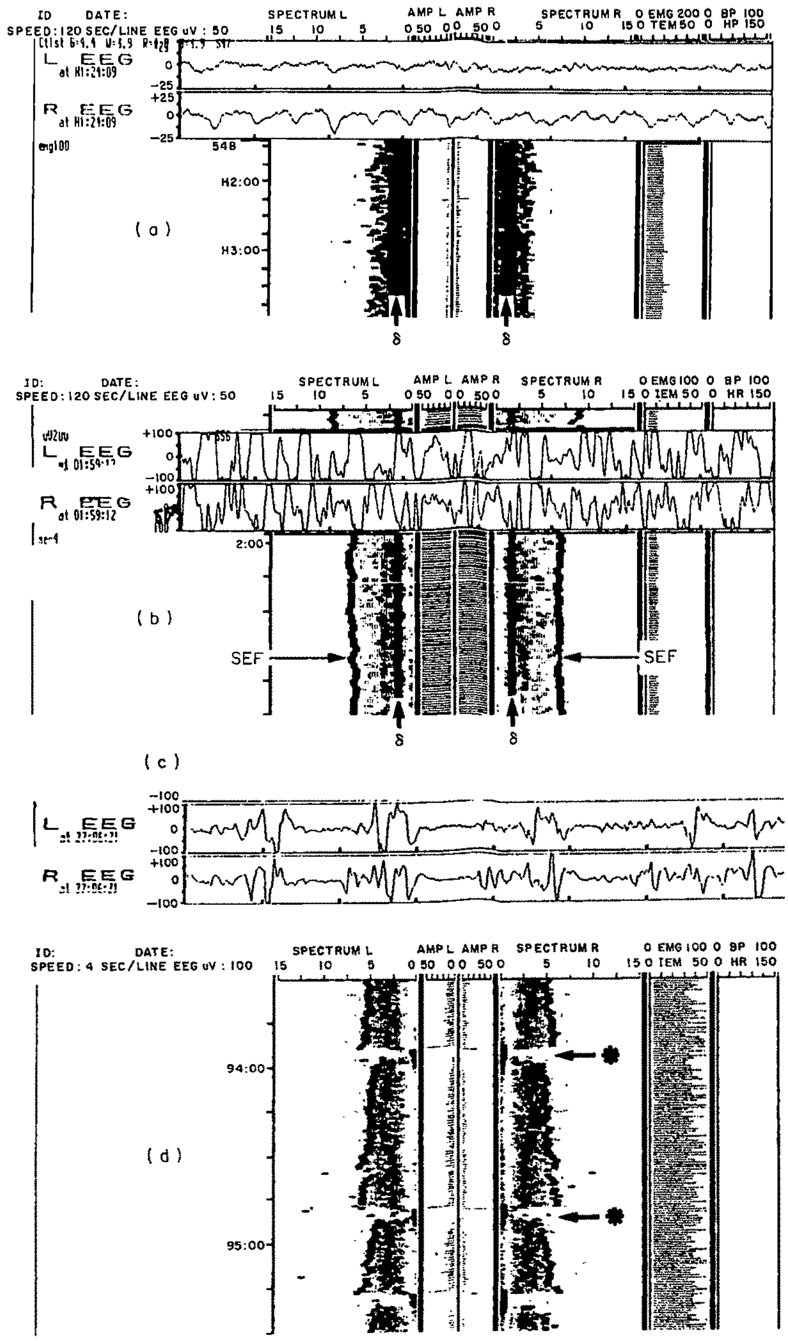

Fig. 3. The EEG tracings (including snapshots of the real time EEG) of a patient from group 2 who appeared deeply sedated with predominant delta activity (compare Fig 2(e)) prior to the sudden onset, (b), of high amplitude discharges (> 100 μv) from both cerebral hemispheres, albeit with significant energy still present in the delta band. (NB, there is a change in the voltage of the real time EEG tracings between Fig. 3(a) and 3(b)). (c) Another patient from group 2 who developed significant spike and wave activity on the real time EEG which corresponded clinically with episodes of facial twitching. (d) At this time the Cerebrotrac 2500 trace showed periods of low frequency electrical activity interrupted by periods of electrical silence(*).

atracurium 1.0 mg/kg/hour, developed sudden onset of grand mal activity, evident both electroencephalographically and clinically. The EEG changed abruptly from a picture of deep sedation (SEF 5 Hz; amp 10–20 microvolts with a large delta component; Fig. 3(a)), to that shown in Fig 3(b) with a SEF of 7–10 Hz and amp > 100 microvolts, but retaining a significant amount of energy in the delta band. The EEG suggested that the convulsive activity was mainly from the right cerebral hemisphere, although this was not apparent from the section of recording shown in Figure 3. The CT scan showed a large right frontal intracerebral haematoma of recent origin.

The nursing staff noticed that a second patient, who was receiving atracurium 0.4 mg/kg/hour, had developed a slight facial twitch. The EEG was also noted to have changed; it showed spike and wave activity which corresponded in time with the facial twitching (Fig. 3(c)). The infusion of atracurium was stopped and once muscle power

began to return there was obvious generalised myoclonic fitting, thought to be the result of a hypoxic cardiac arrest suffered 5 days previously. The Cerebrotrac trace showed a spike and wave pattern, interspersed with electrical silence (Fig. 3(d)).

Discussion

The Cerebrotrac 2500 proved to be a robust and reliable ICU monitor. We did not encounter any equipment failure during the study period: once set up and running the monitor required no further adjustment. The only practical problem was the maintainence of good electrical contact with the patient. Thus there were long periods, usually overnight, when electrical contact was poor, leading to the loss of a meaningful signal. The error was only corrected when one of the authors checked the electrode impedance and reapplied conductive jelly, a simple procedure taking only a matter of minutes. It is envisaged that this task could be delegated to the nursing staff so that periods of poor contact would be reduced and, as a result, the standard of monitoring greatly improved.

The monitor did prove useful in the management of widespread convulsive activity in two patients. Although the patients concerned were receiving continuous infusions of atracurium, the fitting was evident clinically because paralysis was not complete; the EEG therefore offered only supportive evidence of the diagnosis. The real value of the monitor became apparent when the neuromuscular block was deepened using other muscle relaxants in order to ablate all muscular activity; it was then possible to determine the effectiveness of treatment based on the EEG picture. This is very important as it has been shown that electrical fitting, even when not clinically manifest because of neuromuscular paralysis, can cause ischaemic damage to the cerebral cortex.[13] As a result of the limited number of electrodes used to record the EEG signal, it is not possible to localise epileptiform activity to any greater degree than to assign it as being predominantly right or left sided and it is conceivable that a small irritable focus not lying directly under the electrodes may go unnoticed.

A second deficiency of EEG monitors which utilise frequency domain analysis, such as the Cerebrotrac 2500, is the limited amount of fine detail which can be reproduced. This is because the data processing technique requires all events occurring within a single epoch to be averaged. This leads to a potential loss of short-lived events, such as an occasional spike and wave complex. The ability of the monitor to detect early signs of cerebral irritability is therefore questionable. This limitation is reduced by the facility to view and record the raw EEG signal, albeit only when suspicion has been roused.

Lack of familiarity, as with all new monitoring techniques, initially made the medical and nursing staff wary of the usefulness of the monitor. Towards the end of the study, as confidence in interpretation grew, we found increasing use being made of the Cerebrotrac 2500 when deciding, in particular, on adequacy of sedation.

There was possibly a tendency to give excessive sedation to the patients receiving neuromuscular blocking agents (group 2). This frequently resulted in EEG patterns similar to those shown in Figs 2(e) and 2(f), which, in the unparalysed patient, would be considered to be associated with oversedation. It is conceivable that the use of the Cerebrotrac 2500 in those patients receiving muscle relaxants may allow the level of sedation to be adjusted more accurately to the patients needs, thus avoiding oversedation and facilitating patient recovery when the neuromuscular blocking agent is stopped.

Although we used a modification of the Shelly score in order to assess sedation clinically, with the allocation of four levels in the unparalysed group, there appeared to be six distinct EEG levels of sedation. It is possible that, by observing the DSA EEG pattern in combination with the clinical picture, a more accurate appraisal of sedation may be made than with clinical observation alone.

The day-to-day running costs were mainly the result of replacement of ink-jet cartridges. In an attempt to limit the use of both ink and paper we restricted our hard copy printout to 6 hours per page. This achieved the aim of financial prudence, although at the expense of a further loss of detail. A better solution would have been to download the data onto a computer database, the software for which is supplied with the monitor. Not only would this have been cost effective, but it would have enabled the information to have been reprocessed at a later date, improving the diagnostic power of the system.

Continuous EEG monitoring on the ICU, although theoretically attactive, has been mainly confined to neurosurgical units and has not gained widespread acceptance. The reasons for this include difficulties with interpreting processed data and prohibititive cost. The improvements in microelectronics and data presentation combined with competitive pricing of newer EEG monitors, has necessitated a reappraisal of the situation. We found the Cerebrotrac 2500 to be a reliable and affordable monitor which proved to be particularly useful in assessing the adequacy of sedation and in the diagnosis and management of convulsive activity. In general it was considered to be a valuable addition to the ICU monitoring armamentarium.

Acknowledgments

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APPARATUS

The Extensometer

Potential applications in anaesthesia and intensive care

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Summary

The Extensometer is a new device capable of continuous accurate measurement of length over convex surfaces with a rapid response rate. This makes it a powerful research tool and a useful clinical instrument, particularly in the field of respiratory monitoring. This paper describes the principles behind the device. The linearity of its response was demonstrated in laboratory tests and its ability to quantify abdominal and chest wall movement was assessed in anaesthetised patients. Potential applications in the field of ventilatory pattern analysis and respiratory monitoring in anaesthesia and intensive care are discussed.

Key words

Measurement techniques; extensometer.
Monitoring; ventilation.

The Extensometer or 'rubbery ruler' is a new device capable of very precise and rapid measurement of length over convex surfaces, such as the body trunk. It has been produced by the School of Physics at the University of Melbourne and has many potential applications in anaesthesia and intensive care, both in research and clinical practice.

The extensometer comprises a length of silicone rubber which encases two coiled wires that behave like a variable parallel-plate capacitor when stretched. The extensometer with which we were supplied was 4 mm in diameter and 288 mm in length, but other sizes are available. The device is connected to an oscillator to give an output square wave with a frequency which is related directly to length. Signal processing converts this frequency into a filtered analogue voltage which can be measured by a simple voltmeter. Length changes as small as 1 μm can be resolved. Resolution is noise-limited to approximately 0.1 μm. The extensometer is most accurate when stretched by between 5 and 20% of its original length and may be damaged if it is stretched beyond this range. The electrical signal produced, once calibrated, is related linearly to changing length; consequently, real length changes can be monitored accurately (personal communication, Alberto Cimmino, European patent application number 906 30 023.1). The extensometer, voltmeter, oscillator and Velcro bands required for attachment to the patient are shown in Figure 1.

Methods

Laboratory tests

The device supplied by the University of Melbourne was stretched through a series of known static lengths in 2.5-mm increments to between 4 and 17% more than its original length. The voltage output was recorded. This was repeated five times by a single observer and assessed using linear regression analysis.

Clinical tests

Ten patients, ASA 1–2, scheduled for elective peripheral surgery were selected at random. Informed consent was obtained and surgery took place in the supine position. Anaesthesia was induced with propofol and the patients were paralysed with vecuronium. The trachea was intubated, and the lungs were ventilated using an Ohmeda 7000 ventilator at 10 breaths/minute with an inspiration: expiration ratio of 1:2. Anaesthesia was maintained with 30% oxygen in nitrous oxide, and enflurane. Monitoring included capnography, electrocardiography, tidal volume, indirect blood pressure measurement and peripheral nerve stimulation. The train-of-four was maintained at one twitch or less.

The extensometer was connected to a rigid fabric band with Velcro attachments and was attached around the chest

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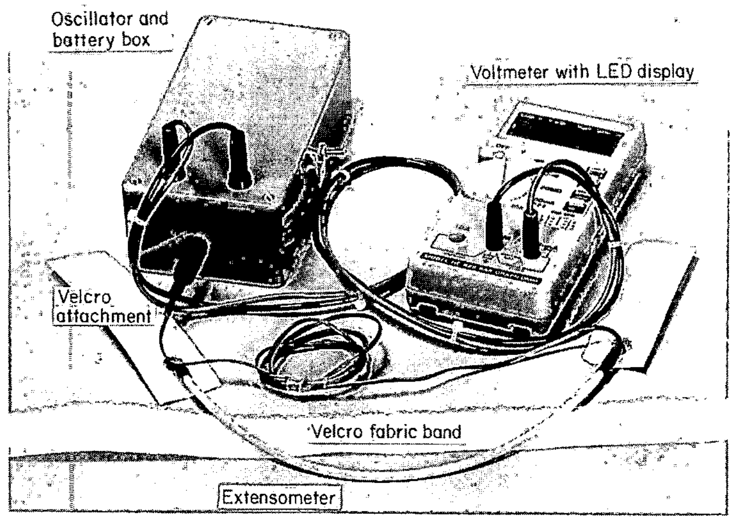

Fig. 1. The extensometer, oscillator and voltmeter with LED display.

immediately above the nipples. A second extensometer was attached at the level of the umbilicus (Fig. 2). The Velcro fastenings were adjusted so that a stretch of 5% was obtained at end-expiration (as measured by the voltmeter using data obtained in the laboratory testing; see Fig. 3).

The lungs were ventilated at tidal volumes of 200, 400, 600, 800 and 1000 ml as measured by an Ohmeda 5400 tidal volume monitor which, according to the manufacturer's specifications, is accurate to within 8%. A multichannel chart recorder running at 5 mm/second and with a gain of 20 mV/mm produced a hard copy of the data.

The trapezoid rule was used to determine the area under the curve (AUC) during each breath both for the chest (AUC-C) and for the abdominal tracings (AUC-A). AUC-C and AUC-A for each tidal volume were added to produce a total AUC (AUC-T). Mean peak voltage changes for chest ($V_{max}C$) and abdomen ($V_{max}A$) at each tidal volume were also noted. The linearities of the relationships between tidal volume, AUC-T, AUC-C, AUC-A, $V_{max}C$ and $V_{max}A$ were examined by regression analysis. $V_{max}C$ and $V_{max}A$ were converted into length changes using data obtained from laboratory tests.

Results

Laboratory tests

The relationship between voltage output and length change over the stretch range of 4 to 17% is shown in Figure 4. The r^2 value for this range was 0.987. No standard deviation (SD) bars have been shown because the mean SD for each 2.5 mm incremental reading was very small (mean 0.016 V, SD 0.01). The relationship between voltage and length at a stretch of less than 4% was found to be less accurate.

Clinical tests

The mean age of the patients was 45 years (range 24–80) and the mean weight was 76 kg (range 55–98). Figure 5 is an example of one of the recordings. The rapid response rate and consistent breath-to-breath relationships are seen easily. Abdominal aortic pulsations can also be seen superimposed on the abdominal tracing and to a lesser extent on the chest tracing.

The extensometer was stretched by 5% of its original length at end-expiration. Tidal volumes of 1000 ml

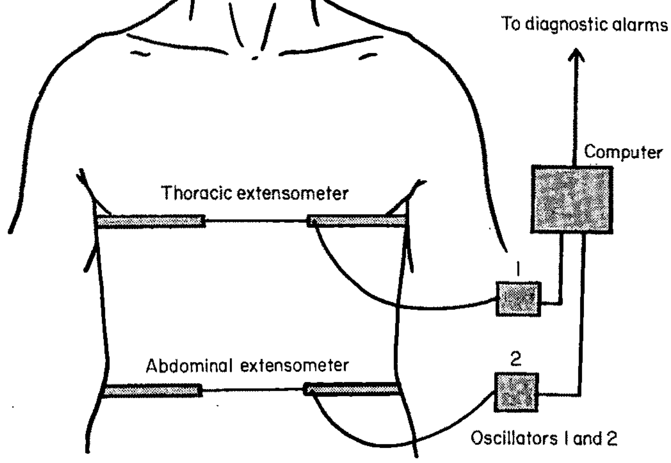

Fig. 2. Two extensometers used to diagnose abnormal respiratory patterns.

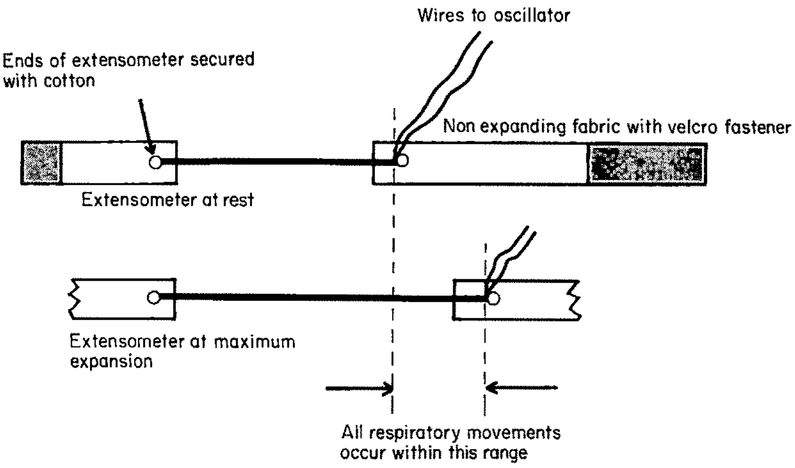

Fig. 3. Use of the extensometer as a respiratory monitor.

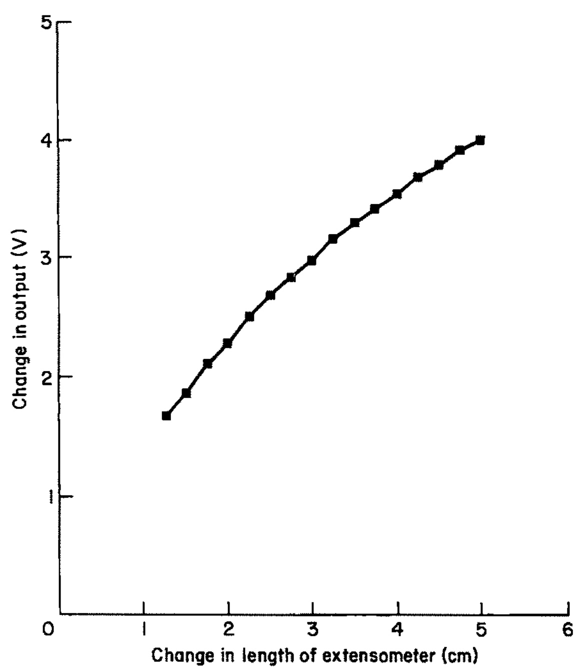

Fig. 4. Mean change in length (cm) of the extensometer ($n = 5$) plotted against change in voltage output (mV). The change in length is equivalent to a change of 4–17% total length. $r^2 = 0.987$. $y = 0.62x + 1.1$.

increased the mean stretch to 6.1% for the chest and 6.3% for the abdominal devices. Over this range the relationship between length and voltage was nearly linear ($r^2 = 0.987$). This corresponded to a mean (SD) maximum circumference change of 0.318 (0.053) cm for the chest and 0.342 (0.061) cm for the abdomen. The relationship between tidal volume and AUC-T for all patients is shown in Figure 6 and was also nearly linear (mean r^2 0.990, SD 0.013). Regression analysis for AUC-C and AUC-A versus tidal volume for all patients confirmed that this was also nearly linear (mean r^2 AUC-C, 0.987, SD 0.009; mean r^2 AUC-A 0.990, SD 0.001). Figure 7 demonstrates the relationship between AUC-C, AUC-A and AUC-T for one patient. The mean ratio of AUC-C to AUC-A was 0.840 (SD 0.388), suggesting that abdominal circumference tends to increase more than chest circumference during intermittent positive pressure ventilation (IPPV). When $V_{max}C$ and $V_{max}A$ are converted into lengths it can be shown that the relationship between change in circumference for both chest (r^2 0.996) and abdomen (r^2 0.998) is related linearly to tidal volume during IPPV (Fig. 8).

Discussion

The results of the laboratory tests confirm that the relationship between length and output voltage is virtually linear

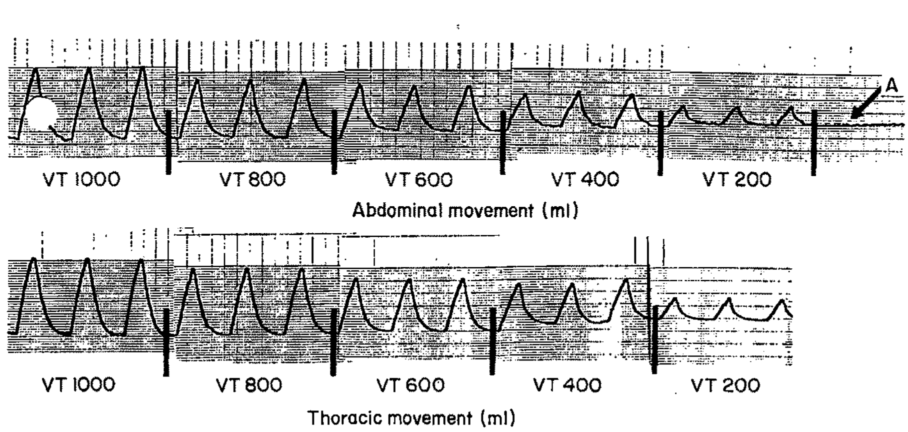

Fig. 5. An example of a tracing from the extensometer showing abdominal and chest wall movement. A = abdominal aortic pulsations. Speed 5 mm second; gain 20 mV/nm.

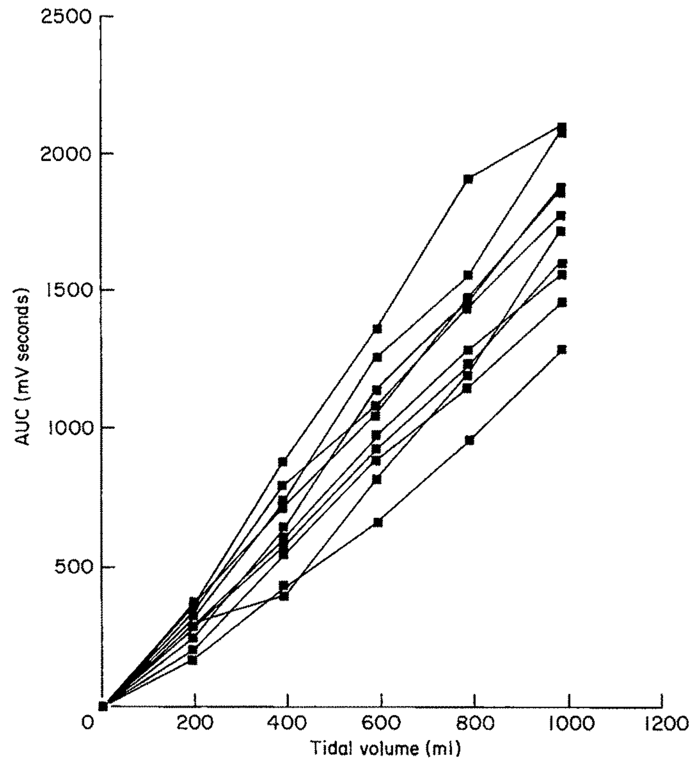

Fig. 6. Tidal volumes (ml) of 10 patients plotted against total area under the curve (AUC-C+AUC-A) (mV seconds). Mean $r^2 = 0.990$, SD 0.013.

over the stretch range 4–17%. These results correlated well with work produced by the School of Physics at the University of Melbourne. Outside this range the relationship is less precisely linear but can be linearised using calibration data and a simple equation (personal communication, Dr Alberto Cimmino, University of Melbourne). It is doubtful whether such mathematical processing would be required in clinical practice. The rapid response rate and repeatable voltage outputs for a given stretch were also confirmed.

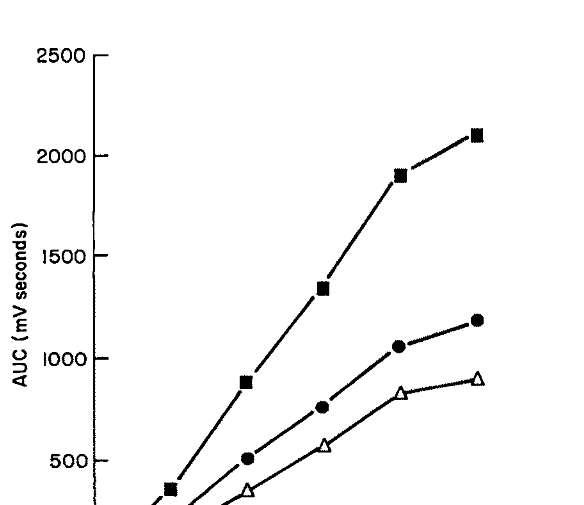

Fig. 7. Tidal volume (ml) of one patient plotted against AUC-C ($r^2 = 0.985$), AUC-A ($r^2 = 0.980$), AUC-T ($r^2 = 0.989$). ■, chest plus abdomen; ●, abdomen; △, chest.

The extensometer was portable, and clinical testing demonstrated that it was easy to use. When placed around the chest it provided continuous readings with minimal baseline wandering, although some diathermy interference occurred.

The clinical study performed with the device demonstrates that there is a linear relationship between tidal volume and thoraco-abdominal movement during IPPV. This relationship holds true for AUC-T, AUC-C, and AUC-A. In addition, $V_{max}C$ and $V_{max}A$ were related linearly to tidal volume and using the data from our laboratory testing we have established that the relationship between tidal volume and change in either chest or abdominal circumference is linear during IPPV. This linear relationship has previously been established only for ribcage movement during spontaneous ventilation in awake patients.[1]

Several techniques have been used by researchers to quantify thoraco-abdominal movement. Such techniques include stereophotogrammetric analysis,[2] X–Y recorders,[3] a combination of inductive plethysmography, magnetometry and mercury-in-rubber strain gauges,[4] and more recently an ultrafast computerised tomographic scanner called the Dynamic Spatial Reconstructor.[5] These devices, although accurate, are impractical in a clinical setting and not useful for continuous monitoring of ventilation.

Transducers placed on or around the torso provide a more practical method of respiratory monitoring and include respiratory inductive plethysmographs,[6] bellows pneumographs,[7] impedance pneumographs,[8] magnetometers,[9] mercury-in-silastic strain gauges,[10] and piezoelectric film belts.[11] With the exception of the impedance pneumograph, these transducers may be calibrated to give approximations of tidal volume using principles laid down by Konno and Mead.[12]

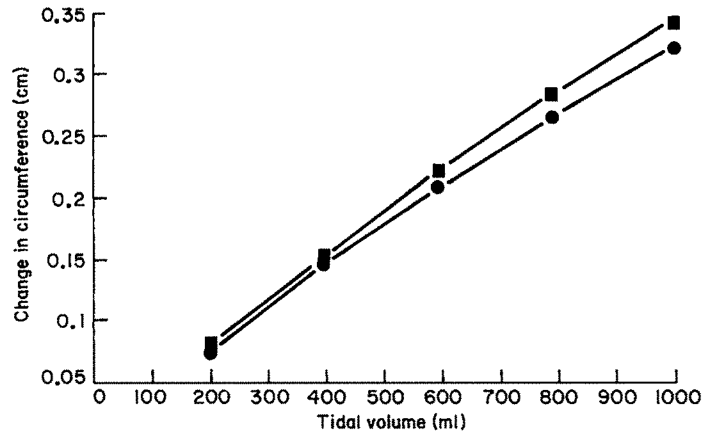

Fig. 8. Mean change in circumference (cm) for chest (●) ($r^2 = 0.996$) and abdomen (■) ($r^2 = 0.998$) plotted against tidal volume (ml).

Respiratory inductive plethysmography (RIP) was introduced in 1977 and is the only technique which has been used extensively in a clinical setting to assess thoraco-abdominal movement.[12] The respiratory inductive plethysmograph consists of two coils of Teflon-insulated wire sewn into elastic bands which are placed around the chest and abdomen. The wires from each band are connected to an oscillator module that produces a low amplitude sine wave. Respiratory movement produces variations in self-inductance, which changes the frequency. This frequency change is demodulated to produce analogue waveforms which reflect accurately changes in the cross-sectional area they enclose.[13] Once calibrated, the plethysmograph yields results within 20% of spirometric tidal volume in awake patients despite changes in posture.[12] It can also be calibrated during IPPV using known tidal volumes, although this has been verified only in lambs and piglets.[14,15]

To our knowledge there are no studies demonstrating the accuracy of RIP during IPPV; consequently, direct comparison with the extensometer is difficult at this stage. However, there are many similarities between RIP and the way the extensometer might be used as a respiratory monitor. When the extensometer is placed around the chest or abdomen, respiratory movement can be quantified accurately with respect to either changing circumference or AUC during IPPV. This system works best, however, when using two extensometers, one around the ribcage, the other around the abdomen, enabling relationships between chest and abdominal movements to be compared (Fig. 2). During spontaneous ventilation the extensometer could in theory be calibrated with respect to tidal volume by using either the Konno-Mead principle or perhaps by using a mathematical model suggested by Faithfull *et al.*[16] Like RIP, multiple inputs could be analysed by computer to allow early diagnosis of abnormal breathing patterns such as the paradoxical movement which occurs in airway obstruction. This system may be of use in postoperative recovery areas where it could be used to distinguish between obstructive and central apnoea. In the intensive care unit the extensometer could be used to help in the diagnosis of various causes of respiratory failure such as upper airway obstruction, diaphragmatic dysfunction, central respiratory dysfunction and excessive respiratory work. The device also has potential as a neonatal and infant respiratory monitor, both in the analysis of respiratory patterns and the rapid detection of apnoea.

The extensometer is sufficiently sensitive that, during apnoea, alterations in thoracic girth due to myocardial contractions may be detected. In thin subjects both abdominal aortic and femoral arterial pulsations can be observed. These findings may have an application in cardiovascular monitoring. The extensometer may be able to remove observer error from the measurement of serial abdominal girths in the cases of suspected intra-abdominal bleeding.

In conclusion, the extensometer is a new device capable of accurate and rapid measurement of length over convex surfaces. It has a potential application in the field of respiratory monitoring. The device certainly merits further investigation and its use in the measurement of awake spontaneous ventilation will be of interest.

Acknowledgments

We thank Dr Alberto Cimmino of the School of Physics, University of Melbourne for providing us with an extensometer.

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APPARATUS

The Alton Dean pressure infusor: an evaluation

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Summary

An automatically pressurised infusor system, the Alton Dean infusor, has been compared with two types (cloth and plastic) of commonly used pneumatically pressurised bags. All the infusors had reasonably accurate pressure gauges but pressure could only be consistently maintained with the cloth infusors or with the Alton Dean infusors when connected to a compressed air supply. Sequential fast infusions were possible with all infusors, but simultaneous infusions could be limited in number when the pressure infusor was connected directly to pipeline gas. One of the Alton Dean pressure infusors tested had a leak in the pressurisation system, and the pressure adjustment valves were difficult to manipulate. These may require modification.

Key words

Equipment; infusion systems.

Rapid infusions of fluid may be required in the operating theatre, recovery room, intensive care unit and wherever emergencies are treated. Various devices have been designed to improve the rate of infusion of fluids, especially those such as blood, which are more viscous than crystalloids; this is commonly performed by pressurising the outside of a flexible bag containing the fluid. If there is no air in the bag, it is a relatively safe method. Cloth bags containing manually or automatically inflatable rubber bladders are available from different manufacturers.[1,2] A clear, thick plastic pressure infusor which has a similar mechanism is an alternative.[3] Rigid enclosures around a pressurised system have also been manufactured and tested,[4–6] and the Alton Dean pressure infusor is a recent development in this range. All systems are available for 500 ml or 1000 ml infusion bags.

This study was designed to test the Alton Dean system with regard to establishing and maintaining fluid infusions, and to compare its advantages and limitations with alternative methods.

Materials and methods

Three types of 500 ml infusors were tested. The first, the Alton Dean pressure infusor* is shown in Figure 1. It consists of a sturdy white box ($10 \times 14 \times 27.5$ cm^3) with a hinged transparent door which is easily opened and closed. There is a hook on the door to hang the fluid to be infused. When the door is closed this is pressurised between the door and a heavy duty polyurethane bladder. The box hangs with an oval handle and mounted above the door is the pressure gauge and pressure regulator. At the base of the infusor is an on/off switch which inflates or deflates the unit. A 3-m tube connects the infusor to an air or oxygen outlet at 4 kPa.

An example of the cloth and rubber infusor† is shown in Figure 2. A nylon net (13×19 cm^2) is attached on two sides to material surrounding a rubber bladder which connects to a pressure gauge and either a manual or automatic pump with a release pressure valve. A bag of infusion fluid has to be passed between the net and bladder, like fitting a sleeve, and is fastened in position by a looped tape which hooks onto an infusion stand.

Figure 3 shows the C-Fusor.‡ This is a clear plastic oval cuff (22×20 cm^2) with arms which wrap with Velcro fastenings around the fluid bag to be infused. The cuff is connected by plastic tubing to a three-way tap which can be opened to air or to a manual or automatic pump. The pressure gauge is connected directly to the cuff.

The 1000 ml infusors were similar to the 500 ml infusors except in dimension, and the pressurised cuffs were all as large or larger in dimensions than the empty flat bags of infusion fluid. Three (2×500 ml; 1×100 ml) Alton Dean

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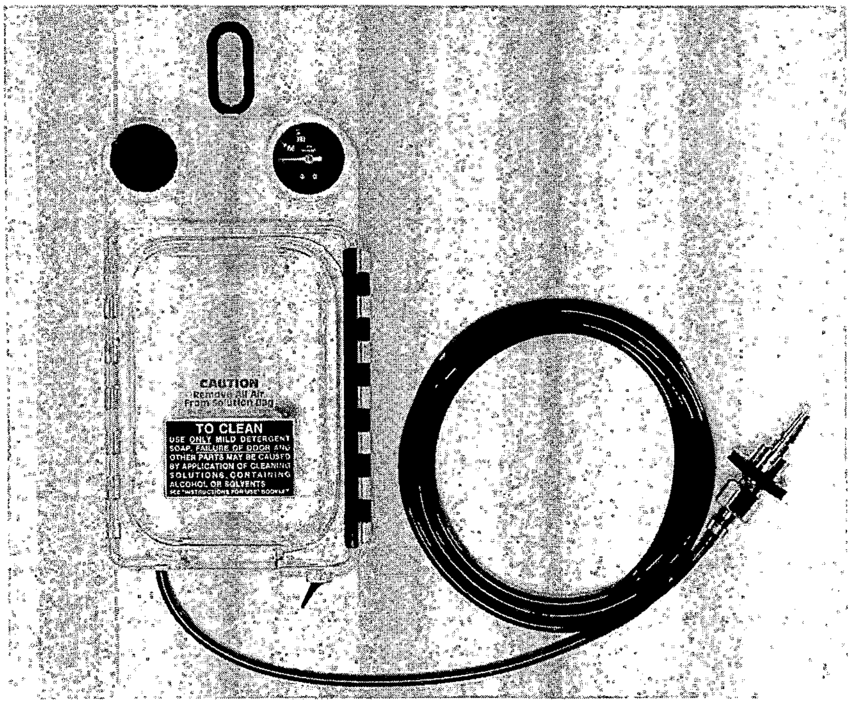

Fig. 1. A 500 ml Alton Dean pressure infusor.

infusors were used directly from the manufacturer but both new and old cloth (new 1 × 500 ml, 1 × 1000 ml; old 2 × 500 ml, 1 × 1000 ml) and plastic (new 1 × 1000 ml; old 1 × 500 ml, 1 × 1000 ml) infusors were available so these were used for comparison.

The pressure gauge of each infusor was checked for accuracy. The pressure cuff was blown up to a recorded pressure of 300 mmHg on the dial and this was connected by a three-way tap to a strain gauge pressure transducer-(Consolidated Electrodynamics) calibrated by 100 mmHg column, and the pressure measured directly. The pressure inside the Alton Dean plastic bladder could not be measured directly, so the pressure inside an infusion bag filled with 50 ml of air was measured when it was positioned inside the pressure chamber adjacent to the plastic bladder inflated to 300 mmHg. Maintenance of pressure in the infusion systems was assessed by inserting a bag full of fluid and then measuring the gauge pressure after 30

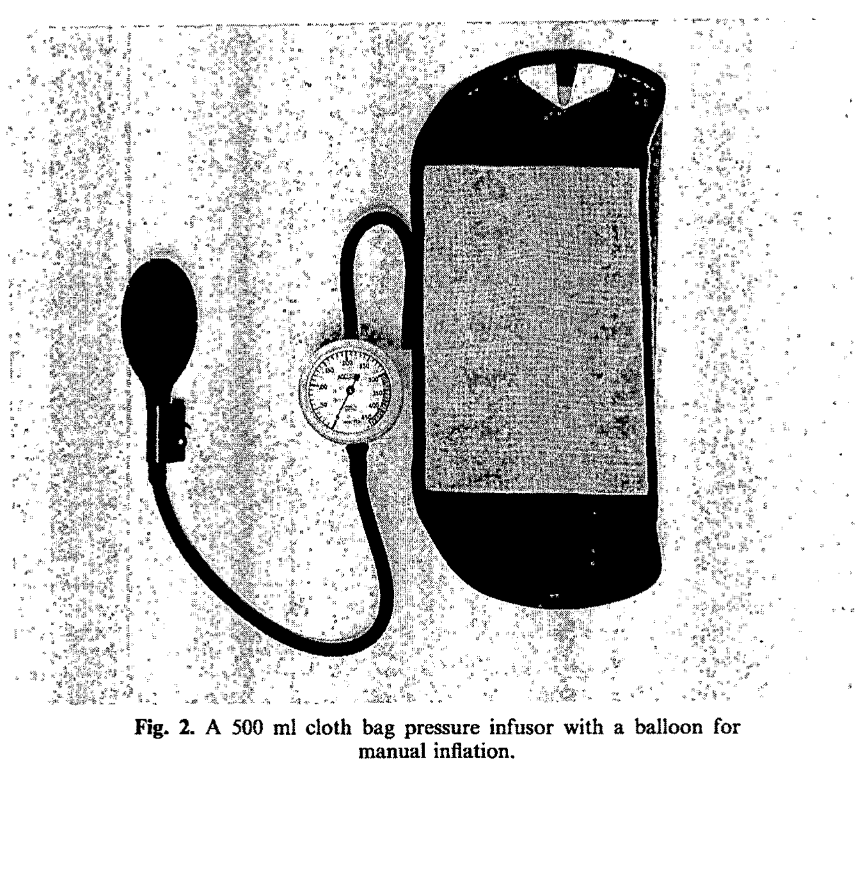

Fig. 2. A 500 ml cloth bag pressure infusor with a balloon for manual inflation.

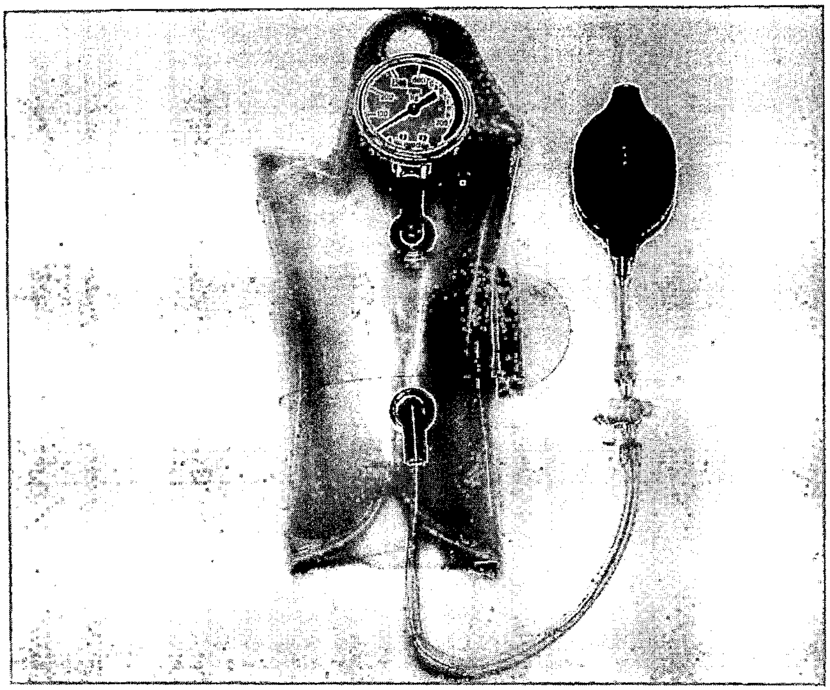

Fig. 3. A 500 ml plastic infusor with a three-way tap connected to a balloon for manual inflation.

minutes. This was to mimic situations where the device was used to flush solutions, to transport patients or just to maintain an infusion ready for use. Wherever there were audible leaks, these were corrected, and the Alton Dean infusors were disconnected from the source of gas for this experiment.

The time spent in changing fluid bags from deflation around one bag to inflation around a second bag, and the times to set up and infuse a bag of fluid have been measured in previous studies.[4,5] The times measured in this study, using 500- or 1000-ml crystalloid solutions as appropriate, were: time (1) setting up an infusion at 300 mmHg; time (2) maintaining the infusion pressure at 300 mmHg with a full bag of fluid to the time when it was emptied; and time (3) deflating the system from 300 mmHg with an empty fluid bag in place. Five operating theatre volunteers were used and during each of the studies any difficulties encountered in using the infusors was noted.

Results

The accuracy of the gauge pressures is recorded in Table 1. Five cloth infusors were tested and two had values of 300 mmHg. These were the two new infusors. All the cloth infusors maintained these pressures for 30 minutes. The plastic infusors had reasonably accurate gauge pressures, but there was a leak in all of them at the junctions of the three-way tap. When used clinically a clamp is used between the infusor and the tap. Two of the Alton Dean infusors measured gauge pressures were consistently slightly lower than the recorded pressures on the gauge. This may reflect the indirect method of measurement. The 500 ml infusion boxes maintained this pressure for 30 minutes when disconnected from the oxygen supply, but the 1000 ml infusion box did not. This has been reported to the manufacturer. However, for prolonged transport applications a hand pump is available for the 1000 ml model, but this was not supplied.

Time (1), the time to fix the fluid bag and generate 300 mmHg pressure in cloth and plastic infusors varied from 40 to 50 seconds. The Alton Dean infusor took half this time unless there was difficulty in connecting the outlet connector into the air or oxygen pipeline terminal. This occurred in two of the five volunteers for one of the infusor boxes and may have been the result of individual equipment variation. The pressure regulator on the Alton Dean infusor rarely needed manipulation, but when it was necessary, it required time and patience. The knob had to be pulled out and held in this position while it was turned. This increased the pressure in the bag but the response was slow so there was a tendency to overinflate the bag. The pressure regulator did not have the facility to reduce the pressure. This had to be effected by switching the infusor off.

Time (2), the time spent in maintaining a pressure of 300 mmHg while the fluid was emptying was only required for

Table 1. The pressure (a) measured when the pressure gauges read 300 mmHg; (b) change in the gauge pressure over 30 minutes for the three types of infusion systems. Values are expressed as mean (SEM) and (range).

Type of infusor	Number	Pressures (mmHg) (a) Measured	(b) Change in pressure
Cloth	5	275 (9) (250–300)	0
Plastic	3	310 (13) (295–335)	−233 (17) (−200–250)
Alton Dean	3	298 (7) (260–310)	0

Table 2. The advantages and disadvantages of the pressure infusors tested.

	Cloth	Plastic	Alton Dean
Cleaning	Difficult	Easy	Mainly easy
Cost	Cheap	Moderate	Expensive
Pressurisation			
Manual	Slow	Slow	Not applicable
Automatic	Fast	Fast	Fast
Maintenance	No leaks	Leaks	Variable
Adjustment	Easy	Easy	Difficult
Fluid			
Fixation	Care required	Easy	Usually easy
Expulsion	Complete	Not complete	Complete
Simultaneous infusions	Available	Available	Needs development
Sequential infusions	Available	Available	Available

the cloth and plastic infusors. The volunteers spent 40 to 50% of their time maintaining the pressure manually, and the system required full time observation. This could be reduced to zero by connecting the bags to an automatic pneumatic pressurising device. The deflation time (time 3) was also similar with regard to the cloth and plastic infusions: 15 to 20 seconds and required both hands, but it was less than 5 seconds for the Alton Dean infusor and required only a switch to be activated.

The advantages and disadvantages observed during the study are recorded in Table 2.

Discussion

The cloth and plastic pressure infusion devices used in this study are widely available and their characteristics for rapidity of onset and reduction of maintenance time can be improved by using an automated pressurising system[1,2] and by incorporating them in a rigid container.[4,5] The ideal infusor would be one that was quickly set up and deflated and required no maintenance time. It should provide surfaces which allow fluid contents and writing on the bag to be visualised, and which are easy to clean, and accurate pressure gauges to which the pressure in the fluid bag can be related. The purchase and running costs should be reasonable and relate to functional life span, so that infusors which are expensive to purchase are rugged and can perform well for many years. Additional equipment such as automated pressure devices may be dedicated to the pressure infusors, or, in the case of tourniquets, be a shared purchase.

There was a tenfold difference in price between the cheapest cloth infusors and the Alton Dean pressure infusor and whether or not this will reflect a life span for the latter requires further investigation. However, five cloth infusors were available which had been purchased over a year ago. Two of these were not used in the study because one pressure gauge had been broken and one cloth covering was heavily stained with blood. Cloth bags can also be torn and the rubber components perish. The plastic infusors are intermediate in price and those in use showed signs of wear in the tubing connecting the three-way tap to the pressure bag. This was the point where they had to be clamped in clinical practice because of a pressure leak from this tap.

The pressure in the gauges during setting up and maintaining a fluid infusion was not accurate in the old cloth infusion bags. However, where gauges are accurate, they are known not to reflect the pressure of the fluid infused,[3,7] and when cardioplegia is given,[8] maintenance of a set pressure is important. There was no alarm system fitted to any of the infusors to detect when the set pressure had become too high or too low. Neither was it possible to know how much fluid had been infused before a fluid infusion bag had been emptied. It was difficult in the case of the cloth bags to have a clear view of the contents of the bag and its label. This could lead to an incorrect infusion being given because it could not be checked once it was set up, without reducing the pressure and withdrawing the bag from the sleeve.

The Alton Dean pressure infusor was preferred to the manual or automatically pressurised bags because it was easier and faster to set up. The times measured in this study compare with those of Chapman and Keep[4] who found it twice as fast to set up and infuse with a pressurised box than a pressurised bag, and in another study,[5] with the number of bulb squeezes. It is possible to connect cloth and infusors in parallel with a single automated pressure device when simultaneous multiple infusions are required. This is clinically our method of choice.[1] The Alton Dean pressure infusor requires further development to allow this since at present only one infusor can be fitted into an oxygen or air pipeline outlet. This would limit its use in most theatres. The Alton Dean pressure infusors are used in the Level 1 blood warmer for consecutive multiple infusions[9,10] where two infusions are connected via a Y-piece into a blood warming system.

Rigid pressure infusors have been available for over 10 years, but still, in practice, the cheaper cloth bags are purchased. The Alton Dean system requires long term evaluation, but it can be recommended where single fast infusions are required, or where pressure maintenance around a fluid infusion is important.

Acknowledgments

We thank Mr A. Wilson of Linx Medical Systems Ltd for supplying the Alton Dean pressure infusors, M and N Surgical for the new cloth pressure infusors, T. Wilkinson SODA, for assistance in testing the systems and Ms B. Williams for secretarial assistance.

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APPARATUS

The use of the Penlon Nuffield 200 in a monoplace hyperbaric oxygen chamber

An evaluation of its use and a clinical report in two patients requiring ventilation for carbon monoxide poisoning

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Summary

We modified a Penlon Nuffield 200 for use in a monoplace hyperbaric oxygen chamber by feeding back the chamber pressure to the reducing valve of the Nuffield 200. This provides a compensating mechanism, allowing the ventilator to deliver adequate tidal volumes at pressures of up to 3 atmospheres. We report the laboratory testing of the ventilator and our experience of ventilating two patients with carbon monoxide poisoning. Although compensation is not complete the modification is adequate for short-term clinical use in patients in whom the airway is compromised but who need hyperbaric oxygen therapy.

Key words

Equipment; ventilator, Penlon Nuffield 200.
Hyperbaric; chamber.

Hyperbaric oxygen therapy has been in use since the 1960s[1] and since then there have been continuous developments in the treatment of critically ill patients within a hyperbaric environment. Most studies of methods of controlled ventilation in a hyperbaric environment have focused on very high pressures (up to 30 atmospheres) such as those used at diving sites and have involved the use of multiplace chambers.[2] Monoplace chambers operate at lower pressures of up to 3 atmospheres absolute (ATA) and are particularly useful for carbon monoxide poisoning and gas gangrene. We have minimised the reduction in tidal volume at higher pressures by modifying a Penlon Nuffield 200 for use with a Hyox monoplace chamber and have evaluated its performance with a lung simulator. We have experience of ventilating at pressures of up to 2.5 ATA and report our experience with two patients undergoing hyperbaric oxygen therapy for carbon monoxide poisoning.

The apparatus

The Penlon Nuffield 200 ventilator acts as a time-cycled flow generator which is a pressure transformer.[3] The pneumatic circuit is shown in Figure 1. The ventilator has been modified to allow the chamber pressure to be fed back to the atmospheric side of the reducing valve 'A' so that the supply pressure varies in direct proportion to the chamber pressure. This provides a pressure compensating mechanism which is designed to allow the ventilator to deliver adequate tidal volumes at chamber pressures of up to 3 atmospheres. The driving gas supply is set at 600 kPa during hyperbaric use. The patient valve module is connected directly to the patient airway so that the driving gas (100% oxygen) is respired by the patient.

The apparatus was tested using a British Oxygen Co 'Manley' lung ventilator performance analyser (LVPA). The lung compliance was set at 50 ml/cmH_2O, which approximates the total thoracic compliance of a normal anaesthetised patient.[4] A resistance of 5 cmH_2O/litre/second was selected as this is approximately the airway resistance of an anaesthetised intubated patient.[4] Although the LVPA is known to have limitations compared to the International Standards Organisation model lung,[4] it was chosen because it is a simple instrument which is routinely used to bench-test clinical ventilators.

The inspiratory and expiratory times and respiratory rate were measured using a Penlon respiratory rate computer. The tidal volumes were measured, with and without the pressure compensating device, using a Wright's respirometer. The increased density of gases at very high pressures reduces the accuracy of the Wright's respirometer, but it has been shown to be accurate up to 3 ATA and was therefore considered adequate for this study.[5]

Figure 2 illustrates the apparatus setup within the chamber. The inspiratory and expiratory (I:E) times were set at 1 and 4 seconds respectively and measurements taken at standard flows of 0.25, 0.5, 0.75 and 1 litre/second whilst the chamber pressure was increased in steps of (5 psi to 20 psi) 1 to 2.34 ATA.

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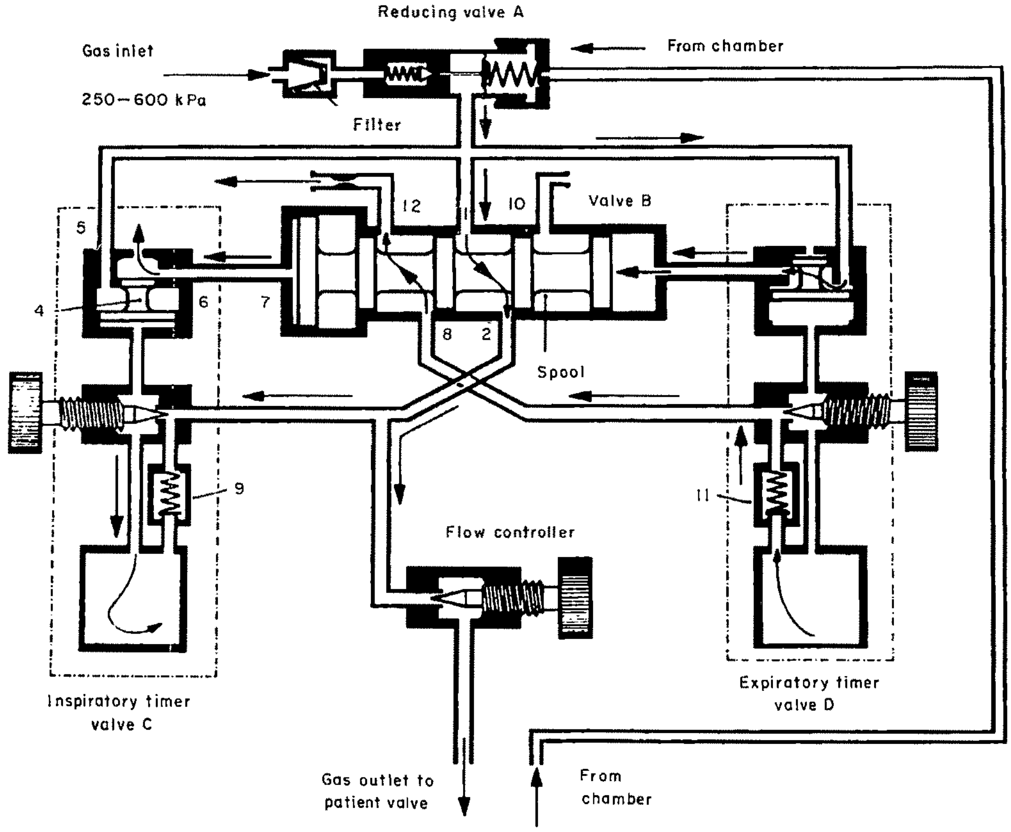

Fig. 1. Pneumatic diagram of modified Penlon Nuffield 200 ventilator.

Results and case histories

The values obtained with the model lung are shown in Table 1 and demonstrate that if inspiratory flow is maintained, satisfactory tidal volumes can be achieved.

The first patient, a 19-year-old male, was referred following an industrial accident when he suffered carbon monoxide poisoning resulting in loss of consciousness and possible pulmonary aspiration of stomach contents. On admission to the primary referral centre the duration of exposure was unknown, but he was unconscious and had a carboxyhaemoglobin concentration of 45%. His trachea was therefore intubated and his lungs ventilated with 100% oxygen. He underwent two hyperbaric oxygen treatments of 90 minutes using the Penlon Nuffield 200. Although he had slight confusion he made an otherwise uneventful recovery and was discharged to the referral centre.

The second patient, a 35-year-old male, suffered self-inflicted carbon monoxide poisoning; the duration of exposure was about 40 minutes. He was unconscious on arrival at the primary referral centre and had a carboxyhaemoglobin concentration of greater than 40%. His trachea was intubated and his lungs ventilated with 100% oxygen before transfer. He underwent three hyperbaric oxygen treatments of 90 minutes each within 24 hours of admission. He was also slightly disorientated but otherwise well and therefore discharged to the referral centre.

Both patients had the cuff of the tracheal tube inflated with saline before being placed in the chamber. The colour of the mucous membranes, chest wall expansion and ECG

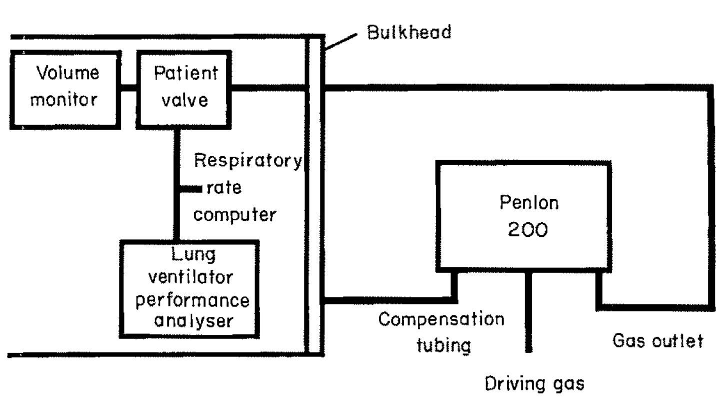

Fig. 2. The layout of apparatus inside and outside the hyperbaric chamber.

Table 1. Values obtained with the model lung.

Flow litres/ second	Chamber pressure; psi	(ATA)	Airway pressure; cmH_2O	Inspiration time; seconds	Expiration time; seconds	Respiration rate/ minute	Tidal volume With compensation; ml	Tidal volume No compensation; ml
0.25	atmos	(1)	12	0.92	4.00	12	220	220
	+5	(1.34)	10	0.86	3.84	13	140	130
	+10	(1.68)	8	0.83	3.76	13	110	90
	+15	(2.00)	7	0.83	3.63	13	100	80
	+20	(2.34)	6	0.80	3.53	14	90	80
0.5	atmos	(1)	33	0.96	3.96	12	420	420
	+5	(1.34)	20	0.80	3.75	13	320	210
	+10	(1.68)	20	0.93	3.68	13	300	210
	+15	(2.00)	18	0.92	3.58	13	290	210
	+20	(2.34)	16	0.92	3.47	14	250	190
0.75	atmos	(1)	50	1.00	3.96	12	580	580
	+5	(1.34)	35	0.96	3.72	13	460	330
	+10	(1.68)	31	0.96	3.66	13	430	340
	+15	(2.00)	28	0.96	3.57	13	400	290
	+20	(2.34)	22	0.95	3.42	14	370	250
1.0	atmos	(1)	55	0.96	3.98	12	660	660
	+5	(1.34)	45	0.98	3.72	13	580	490
	+10	(1.68)	41	0.98	3.66	13	530	390
	+15	(2.00)	36	0.97	3.56	13	490	330
	+20	(2.34)	30	0.95	3.45	14	450	280

was observed by an anaesthetist at all times during hyperbaric treatment. The tidal volume was monitored, using a Wright's respirometer attached to the exhaust port of the patient valve. The inspiratory flow was increased as the chamber pressure rose in order to maintain adequate tidal volumes. The results of the volumes obtained in both patients are shown in Table 2.

Discussion

A method of ventilation within the monoplace hyperbaric chamber needs to be available so that patients who are unconscious and unable to protect their airway may be treated. Our modification of the Penlon Nuffield 200 is a relatively inexpensive and easy to use method and since the ventilator is in common use in our operating theatres there is no difficulty in training junior staff in its use for hyperbaric treatment.

The function of any mechanical ventilator placed outside a hyperbaric chamber will be limited by Boyle's law. As the pressure increases within the chamber, the tidal volumes obtained at each flow diminish. However, when the pressure compensating device is inserted, this reduction in volume is not as great, indicating that although the compensatory mechanism is not completely effective it results in a significant improvement in the function of the ventilator at elevated pressures.

Since the feedback pressure also influences the pressure build-up in the inspiratory and expiratory valves, the compensator reduces the inspiratory and expiratory times. This leads to an increase in the respiratory rate, which results in a smaller reduction in minute volume as the pressure increases. For example, at atmospheric pressure, a flow of 0.75 litres/second and I:E ratio of 1:4 results in a tidal volume of 580 ml and a minute volume of 6960 ml. At 2.34 ATA (20 psi), without the compensator the tidal volume was reduced by 57% to 250 ml, whereas with the compensator the reduction was only 37% (to 370 ml). The beneficial effect of increasing the respiratory rate means that the minute volume was only reduced to 5180 ml (26% reduction), compared to 3500 ml (50% reduction) without the compensator.

Ventilation of the two patients was successful, although we needed to increase the inspiratory flow as the chamber pressure increased, in order to maintain adequate tidal and minute volumes. The minute volume of both patients was 9000 ml before entering the chamber and was maintained at all pressures up to 2.34 ATA (20 psi). This would not have been possible without the modified ventilator. It is essential that the tidal volume is monitored continuously and the flow rate increased to improve the volumes delivered as the pressure within the chamber is increased.

Table 2. Results of volumes obtained in both patients.

Patient 1; Pre-treatment. Tidal volume = 800 ml, rate = 12/minute, inspiration time = 1.5 seconds.

Chamber pressure; psi	ATA	Flow; litres/ second	Tidal volume; ml	Respiration rate/ minute
0	1	0.5	750	12
5	1.34	0.5	725	13
10	1.68	0.75	725	13
15	2.00	1.0	700	13
20	2.34	1.0	675	14

Patient 2; Pre-treatment. Tidal volume = 800 ml, rate = 12/minute, inspiration time = 1.5 seconds.

Chamber pressure; psi	ATA	Flow; litres/ second	Tidal volume; ml	Respiration rate/ minute
0	1	0.5	750	12
5	1.34	0.75	700	12
10	1.68	1.0	750	13
15	2.00	1.0	700	13
20	2.34	1.0	650	14

The mechanism described here, although not providing total compensation, nevertheless results in adequate performance for clinical use in patients in whom the airway is compromised but who need hyperbaric therapy.

Acknowledgments

The authors thank Penlon for their assistance and for the loan of the testing equipment.

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Forum

Comparison of propofol and thiopentone for laryngeal mask insertion

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Summary

Conditions for insertion of the laryngeal mask were assessed following induction of anaesthesia with either propofol 2.5 mg/kg or thiopentone 4.0 mg/kg in 80 patients premedicated with diazepam 10 mg. Insertion following induction with thiopentone resulted in a greater incidence of gagging ($p < 0.01$). The use of additional induction agent, where necessary, resulted in no ultimate significant difference between the groups for the provision of satisfactory conditions.

Key words

Anaesthetics, intravenous; propofol, thiopentone.
Equipment; laryngeal mask.

The laryngeal mask is a new form of airway (LMA),[1] which is introduced blindly into the hypopharynx to form a seal around the larynx.[2] It has been shown to provide a clear airway and leaves the anaesthetists' hands free.[3] In our department the preferred induction agent for insertion of the LMA for general anaesthesia with spontaneous ventilation is propofol. In view of the relative expense of propofol and pain on injection it would be of value to confirm or disprove the advantage of this agent in this respect.

Methods

The study was approved by the District Ethics Committee. Eighty ASA 1 or 2 patients aged 18 to 70 years undergoing surgery for which the LMA was appropriate were studied. Exclusion criteria consisted of a history of asthma and any potential risk of gastric regurgitation.

All patients were premedicated with diazepam 10 mg orally 2 hours before operation. Induction was with fentanyl 1 μg/kg followed by a randomly allocated equipotent dose of either propofol 2.5 mg/kg or thiopentone 4.0 mg/kg, given over 30 seconds. LMA insertion, as previously described,[2] was by another anaesthetist who was unaware which induction agent had been given. Anaesthesia was then maintained with a volatile agent and 66% nitrous oxide in oxygen, with the patient breathing spontaneously through a Bain system. Successful atraumatic insertion requires the abolition of the gag and cough reflexes.[2] The anaesthetist inserting the LMA scored both reflexes using a −, + and ++ system, together with any comments. The necessary use of additional induction agent was also recorded. The anaesthetists varied in experience from SHO to consultant, but all were experienced in the use of the LMA.

Patients' demographic data were also noted and compared between the propofol and thiopentone groups using unpaired *t*-tests and a Chi-squared test. The gagging and coughing scores were compared using Mann–Whitney *U* tests, and the quantity of additional induction agent using a Chi-squared test and a Fisher exact probability test. Yates' correction was applied to the Chi-squared tests. A p value of < 0.05 was accepted as indicative of a significant difference.

Results

There were no significant differences between the groups in age, weight or sex distribution (Table 1). The scoring of conditions for LMA insertion showed a significantly higher incidence of gagging in the thiopentone group ($p < 0.01$) but there was no significant difference in the incidence of coughing ($p = 0.30$) (Table 2).

The use of additional induction agent was significantly greater in the thiopentone group ($p < 0.01$). However, the subsequent failure to provide satisfactory conditions showed no significant difference ($p = 0.999$). The presence of hiccoughs and poor jaw relaxation were noted in eight and 11 patients respectively but with no significant difference between the groups.

Table 1. Demographic data of patients in both groups. Values expressed as total numbers or mean (SD).

	Propofol	Thiopentone
Age; years	45.9 (15.3)	42.8 (13.8)
Weight; kg	70.5 (12.5)	72.4 (16.3)
Males	19	16
Females	21	24

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Table 2. Scoring of conditions for LMA insertion.

	Propofol	Thiopentone
Gagging		
–	38	28
+	1	6
++	1	6
Coughing		
–	37	34
+	1	3
++	2	3

Table 3. Use of additional induction agent.

	Propofol	Thiopentone
Additional induction agent	5	18
Failure to provide satisfactory conditions	1	2

Discussion

This study has demonstrated a significant difference in the incidence of gagging when using an equipotent dose of propofol or thiopentone for insertion of the LMA. Equipotency in this context referred to the production of unconsciousness.[4] Previous work has shown that with subhypnotic doses, propofol and thiopentone have analgesic and antanalgesic actions respectively.[5] Induction of anaesthesia with propofol is accompanied by a greater degree of ventilatory depression than following thiopentone.[6]

The use of additional induction agent, where necessary, resulted in no significant difference between the groups in the provision of satisfactory conditions for insertion of the LMA. This suggests that propofol is either more effective at providing satisfactory conditions or that the doses used were not equipotent for the insertion of the laryngeal mask.

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Nurse-controlled intravenous analgesia

Effective control of pain after thoracotomy

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Summary

Nurse-controlled continuous intravenous opioid analgesia was evaluated prospectively in 60 patients after thoracotomy. The rate of opioid infusion was adjusted, and bolus doses were administered, as required to maintain patient comfort. The patients evaluated their pain using a visual analogue scale on 10 occasions during the first 48 hours after surgery. Pain scores remained consistently low throughout the period of measurement. Over the study period there was a 30-fold difference between the least and greatest requirement for opioid to achieve adequate analgesia. No major side effects were encountered. The study indicates that nurse-controlled intravenous analgesia can be successfully used for pain relief after thoracotomy.

Key words

Analgesia; intravenous, postoperative
Analgesics; papaveretum.

Patient-controlled analgesia (PCA) is increasing in popularity as a method of postoperative pain relief in adults and in children after major surgery. Comparisons with intramuscular opioid analgesia have shown that PCA tends to provide better quality of pain relief.[1-4] Not all patients, however, are suitable for PCA (*vide infra*) and an alternative is to use continuous intravenous analgesia but to establish an improved nurse-controlled technique.

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This hospital has, for approximately 10 years, used continuous intravenous nurse-controlled opioid analgesia to control postoperative pain after major surgery. Morphine 50 mg, pethidine 500 mg or papaveretum 100 mg are diluted to 500 ml in physiological saline or a 5% dextrose solution and given by continuous intravenous infusion through a Travenol Flo-gard 8000 infusion device (Baxter Health Care Corporation, Illinois). Before the acquisition of a sufficient number of infusion devices, the infusion was titrated through a burette which was refilled hourly to contain only that hour's expected total requirement. This was to prevent accidental infusion of a large volume of opioid.

The adequacy of pain relief after surgery using this technique was prospectively evaluated in patients on the first and second days after thoracotomy.

Method

Patients, scheduled to undergo thoracotomy and who gave informed consent, were recruited for this study. Those whose understanding of the English language was limited or who were unable to understand the visual analogue scale which was to be used for pain assessment were excluded from the study. A standard anaesthetic technique (N_2O/O_2/volatile agent/morphine) was used for all patients. On return to the recovery room, a continuous intravenous infusion of papaveretum was commenced. Repeated bolus injections of papaveretum were administered as required by the recovery room nursing staff so that the patients were pain-free on return to the ward. All patients returned to the same ward and were cared for by the same group of registered nurses who were responsible for controlling the opioid infusion rate. Infusion orders were written as a range of infusion rates (usually 20–40 ml per hour) between which the nurse could titrate the opioid. In addition, a bolus injection of 20–40 ml could be administered as often as required to regain pain control if the continuous infusion had initially been insufficient. The infusion rate was titrated to achieve adequate analgesia as judged by the patient. If the highest infusion rate prescribed was insufficient to control pain, the nurse contacted the appropriate doctor to adjust the range of infusion rate allowed. If the patient became excessively drowsy, the infusion rate was reduced so that the patient was always easily rousable. Respiratory frequency was monitored every 5 minutes for 30 minutes after any change of infusion rate and thereafter hourly during intravenous opioid infusion. The patients were asked by one of the authors on 10 occasions in the subsequent 2 days to assess their pain using the 10 cm visual analogue scale.[5] The nurses had no forewarning of the timing of such assessment.

Results

Sixty patients were prospectively enrolled for evaluation of nurse-controlled intravenous analgesia. Eight patients were lost from the study because of their transfer to another ward postoperatively or because of incomplete data recording. The mean cumulative papaveretum requirement for all patients is shown in Table 1.

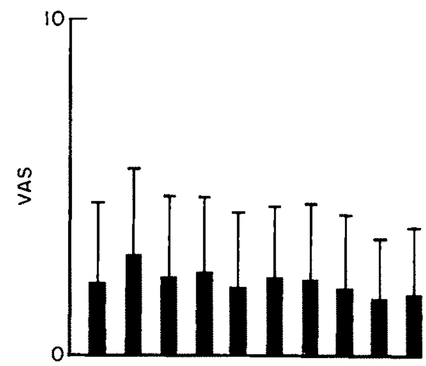

Fig. 1. Consecutive visual analogue scale (VAS) pain scores (mean ± SD) on the first and second postoperative days. See text for details.

The largest amount of papaveretum required over a 48-hour period was 253 mg. The papaveretum requirement varied 30-fold from the greatest to the least over the 48 hours. The total number of bolus injections administered in addition to alterations of infusion rate is also shown in Table 1. The maximum number of bolus injections required by a patient in a 6-hour period was five.

In most cases visual analogue pain scores were elicited six times on the day after surgery and four times on the subsequent day. If the patient returned to the ward by midday on the day of surgery, the first pain score was elicited on that afternoon. Visual analogue scores did not change significantly throughout the period of study (Fig. 1).

Respiratory frequency was monitored hourly throughout the period of nurse-controlled intravenous analgesia and a total of 1929 observations were made during this time. On 38 occasions the respiratory rate was less than 10 breaths per minute. In almost all cases, these were isolated recordings of nine breaths per minute; no specific treatment was required in any case. In most cases it was not considered that a reduction in papaveretum infusion was required.

Discussion

This study indicates that adequate pain relief after major surgery can be achieved using nurse-controlled intravenous analgesia and that this high quality of analgesia can be maintained consistently over the second and third postoperative days.

Pain scores achieved in this study compare favourably with similar studies.[6,7] Asantila *et al.*,[6] comparing five different methods of pain relief after thoracotomy, did not achieve pain scores as low as those found in our study of nurse-controlled intravenous analgesia. Logas *et al.*[7] also

Table 1. Cumulative papaveretum requirement and number of bolus injections included, in each 6-hour period to 48 hours (mean ± SD) (n = 52).

	Hours							
	0–6	7–12	13–18	19–24	25–30	31–36	37–42	43–48
Mean cumulative papaveretum requirement (SD)	25.6 (14.0)	42.3 (24.0)	57.5 (32.2)	72.0 (38.4)	81.4 (42.7)	88.1 (46.7)	92.9 (50.5)	94.7 (51.7)
Number of bolus injections required	35	5	8	14	8	1	1	1

evaluated five methods of pain relief after thoracotomy and only the group receiving epidural local anaesthesia in combination with epidural opioids achieved better pain scores. This study, like ours, also demonstrated that continuous infusion analgesia after thoracotomy provides a consistent quality of pain relief during the period of patient mobilisation and chest physiotherapy.

A recent study by Zacharias, Pfeifer and Herbison[8] in patients after upper abdominal surgery is the first to compare PCA with nurse-controlled intravenous analgesia. The authors found the quality of analgesia to be similar for both techniques but that patients using PCA received significantly less morphine than the other group. They suggest that a small bolus size and a long lockout period might have contributed to this result. We have recently started a similar prospective comparison with a larger bolus size and a shorter lockout period in patients after thoracotomy.

Although PCA is considered by many to be the gold standard for postoperative pain relief, nurse-controlled intravenous analgesia may have some advantages over PCA. Firstly, nurse-controlled intravenous analgesia may be used successfully for all patients after surgery. Despite adequate explanation and understanding of the technique, some patients may be either unwilling or unable to use PCA.[9,10] Factors such as sociocultural characteristics, personality disposition, fear of control of powerful drugs and fear of drug addiction are some of the reasons attributed to the failure of PCA in such patients. Using nurse-controlled intravenous analgesia, such patients can receive adequate analgesia when PCA would have been unsuccessful. Bolus doses can similarly be administered by the nurse in anticipation of such activities as chest physiotherapy and wound dressing.

A feature of nurse-controlled intravenous analgesia which is presently not routinely possible with PCA is the ability to alter the basal infusion rate depending on the needs of the patient. It would appear, for example, that the requirement for analgesia undergoes a diurnal variation and that if a continuous background infusion of opioid is administered in addition to PCA, this infusion may contribute little to improvement in analgesia but increase the risk of oversedation at night.[11] For this reason, there is some debate as to the merits of a background continuous infusion in addition to PCA.[12] Nurse-controlled intravenous analgesia provides the dual capability of altering both the background infusion rate and the bolus size if required.

Potential adverse effects from nurse-controlled intravenous analgesia are similar to those encountered with PCA.[13] However, with set guidelines for administration and monitoring of infusion rates and bolus size and frequency, excessive drowsiness and respiratory depression rarely occur but, when encountered, occur slowly and respond readily to a reduction in opioid infusion rate.

A reasonable criticism of nurse-controlled intravenous analgesia is that it is not directly controlled by the patient. Against this it can be argued that the nurse's end-point in determining the correct rate of infusion for each patient is the patient's satisfaction with the quality of analgesia. In this way it is the patient who determines the rate of infusion albeit indirectly. The number and frequency of bolus injections is similarly determined so that a 'steady state' is more rapidly achieved in line with the pharmacokinetic concept of the 'loading dose'.

Finally the capital cost of purchasing intravenous infusion devices is significantly less than for PCA devices so that more of these can be acquired for a given financial budget. Consequently more patients are in a position to benefit from postoperative intravenous analgesia.

Acknowledgments

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Propofol: bolus or continuous infusion

A day case technique for the vaginal termination of pregnancy

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Summary

Forty patients undergoing vaginal termination of pregnancy were randomly allocated to receive a propofol anaesthetic using either a repeat bolus or infusion technique. The Ohmeda 9000 Infusion Pump was used in the study. Patients in the infusion group recorded significantly longer induction times, greater maintenance doses and prolonged immediate recovery characteristics. Both techniques offered cardiovascular stability but no advantages were demonstrated for the infusion technique over a conventional repeat bolus method.

Key words

Anaesthetics, intravenous; propofol.

Propofol has been extensively investigated for day surgery[1] and may be the anaesthetic agent of choice with the benefit of having a low incidence of adverse effects.[2] Many anaesthetists use a repeat bolus technique when propofol is given for short procedures. This method has disadvantages, particularly the high incidence of patient involuntary movement and difficulty in maintaining a clear airway during surgery.

The introduction of the Ohmeda 9000 Continuous Infusion Pump with a bolus facility prompted us to investigate the suitability of a continuous infusion propofol technique for short day case procedures. The aims of the present study were to assess the practicality of the technique, the ease of administration, the stability of the vital signs and the immediate recovery characteristics.

Method

The study was a randomised, open, between-patient comparison of intermittent bolus and continuous infusion techniques of propofol administration. Local Ethics Committee approval was obtained and informed consent sought from ASA grade 1 or 2 patients presenting to the Day Surgery Unit for vaginal termination of pregnancy (VTOP). The patients were allocated to one of two groups using a randomised allocation code.

Group 1. Anaesthesia was induced with a dose of propofol from a hand-held syringe titrated according to patient response until loss of verbal contact. Anaesthesia was maintained with incremental bolus doses of propofol 30 mg from a hand-held syringe. Boluses were given at the discretion of the anaesthetist in response to clinical signs of light anaesthesia or in anticipation of a surgical stimulus.

Group 2. Anaesthesia was induced with propofol given as a continuous infusion using the Ohmeda 900C Infusion Pump at a rate of 1200 ml/hour until loss of verbal contact. Anaesthesia was maintained with an infusion of 9 mg/kg/hour of propofol; supplementary boluses were given if indicated at 1200 ml/hour.

Intravenous access was secured using an indwelling cannula (23G Y-Can, Wallace) located on the dorsum of one hand. Lignocaine 1% 1 ml was added to each 20 ml of propofol, and the mixture was used within 30 minutes of preparation. All patients were unpremedicated, were anaesthetised in theatre on the operating table and were induced according to group allocation. All received alfentanil 3.5 μg/kg immediately before induction and again immediately before dilatation of the cervix. Patients were allowed to breathe 66% nitrous oxide in oxygen from a facemask attached to a Bain breathing system.

Electrocardiograph (ECG) and oxygen saturation were monitored continuously. Arterial blood pressure was measured noninvasively (Datascope Accutorr); values were recorded before induction, 2 minutes after induction and at the end of the procedure. Immediate recovery was assessed by a recovery nurse who was unaware of which anaesthetic technique had been used. The measurements made were: the time until the patient opened her eyes to command, the time until the patient was able to state her date of birth accurately, and the time until the patient was able to sit up unaided.

Quality of induction was graded by the anaesthetist as either good, adequate or poor and the administration of the anaesthetic graded as easy, adequate or difficult. Statistical analysis was carried out using Student's *t*-test or Fisher's Exact test as appropriate. A p value of less than 0.05 was taken to represent a significant difference.

Results

A total of 40 patients were recruited to the study. Table 1 shows the mean (SD) for the demographic data in the study. No significant differences were recorded between the two groups. Table 2 records the mean (SD) propofol doses used for induction and maintenance. The total maintenance dose given in the infusion group was significantly greater than for the bolus technique ($p < 0.001$) and 14 of the 20 patients in the infusion group required at least one additional bolus of propofol. Both the time for the patient to stop counting at induction and the time to the start of surgery were longer in the infusion group ($p < 0.001$). Table 3 shows the mean (SD) immediate recovery times in

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Table 1. Demographic data and duration of surgery. Values are expressed as mean (SD).

	Propofol	
	Bolus ($n = 20$)	Infusion ($n = 20$)
Age; years	22.6 (5.1)	26.4 (6.9)
Weight; kg	60.4 (7.1)	58.3 (8.7)
Duration of surgery; minutes	6.7 (2.8)	5.9 (1.8)

No significant difference between the groups (Student's t-test).

Table 2. Induction data and propofol doses. Values are expressed as mean (SD).

	Propofol	
	Bolus	Infusion
Induction dose mg/kg	2.65 (0.37)	2.99 (0.40)
Patient stops counting; seconds	43.5 (6.7)	52.5 (6.1)*
Start of surgery; seconds	82.4 (11.6)	96.9 (10.4)*
Maintenance dose; mg/kg/hour	6.98 (3.63)	12.47 (5.35)*

*$p < 0.001$ (Student's t-test)

Table 3. Immediate recovery times. In minutes expressed as mean (SD).

	Propofol	
	Bolus	Infusion
Eyes open	5.1 (1.8)	7.0 (2.9)*
State date of birth	6.3 (2.2)	8.5 (3.3)*
Sit unaided	8.5 (2.7)	10.6 (4.1)

*$p < 0.05$ (Student's t-test)

the two groups. Both the times to eye opening on command and the ability to correctly state their date of birth were longer in the infusion group ($p < 0.05$).

Figure 1 shows the mean (SD) changes in systolic and diastolic pressures. The haemodynamic changes after induction were similar for both groups. At the end of the operation both systolic and diastolic pressures were lower in the infusion group. The difference was only statistically significant for the diastolic pressure ($p < 0.05$). Changes in heart rate were similar in both groups. No bradycardia requiring treatment was recorded in either group. Table 4 shows the anaesthetist's assessment of the quality of induction and maintenance. Both groups were graded as good for quality of induction and maintenance. Ease of administration was graded as easy in all patients maintained by continuous infusion.

Discussion

Propofol is rapidly metabolised and the swift immediate recovery[3] and absence of nausea and vomiting[4] make it an excellent anaesthetic induction agent for day cases. It has proved a useful anaesthetic agent when given by continuous infusion for longer procedures.[5] However, when used by the intermittent bolus technique, more commonly employed for short procedures, there are disadvantages,

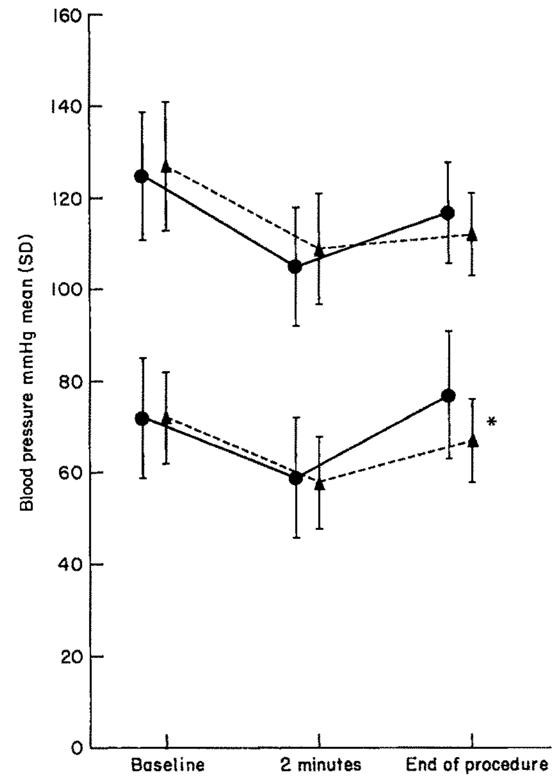

Fig. 1. Changes in systolic and diastolic blood pressure. ——●——, bolus group; — —▲— — infusion group. *$p < 0.05$ (Student's t-test).

such as pain on injection, hypotension, periods of apnoea and rapid lightening of anaesthesia with subsequent patient movement. We investigated a continuous infusion technique with the aim of developing a smoother anaesthetic. However, any advantage would need to be balanced against the additional cost of disposables and extra time involved in setting up the infusion.

The Ohmeda 9000 infusion apparatus proved easy to use and the bolus facility was an added advantage both for inducing the patient and for deepening the anaesthetic during surgery. The infusion apparatus with its giving set took approximately 2 minutes to set up and prime.

The manufacturer's recommended induction dose of propofol is 2–2.5 mg/kg titrated at approximately 40 mg every 10 seconds. In this study of young, fit, healthy, unpremedicated female patients a mean induction dose of

Table 4. Anaesthetists assessment.

	Propofol	
	Bolus	Infusion
Quality of induction		
Good	20	19
Adequate	0	1
Poor	0	0
Quality of maintenance		
Good	15	13
Adequate	4	7
Poor	1	0
Ease of administration		
Easy	18	20
Adequate	2	0
Difficult	0	0

No significant difference between the groups (Fisher's exact test).

3 mg/kg was required. Despite this relatively large dose only moderate haemodynamic effects were observed. The slower administration of propofol at induction might be expected to reduce the total dose required[6] but this was not found in our group of patients.

A dose of 9 mg/kg/hour of propofol was chosen for the infusion group from previous clinical experience and published results.[7] Nevertheless 14 of the 20 patients in the infusion group required at least one additional bolus of propofol in response to patient movement during surgery. The total dose of propofol used was greater in the infusion group and this was reflected in the longer immediate recovery times for that group.

In a previous study of continuous infusion versus intermittent bolus administration of fentanyl or ketamine for outpatient anaesthesia, White reported a greater than 40% reduction in dose requirements for both drugs when given by continuous infusion.[8] However in White's study additional boluses or changes in infusion rate were made only in response to predetermined signs of inadequate anaesthesia. The greater flexibility of our protocol allowed the anaesthetist to give a bolus in anticipation of a surgical stimulus. In this way level of anaesthesia could be tailored to match the rapidly changing levels of surgical stimulation. This may explain the lower total dose requirement in the bolus group in our study.

Another notable difference between these two studies is the duration of surgery. In our study the mean duration was 6 minutes compared to 22 minutes in White's paper. It seems likely that any advantage of continuous techniques over intermittent bolus methods will be more apparent in longer procedures.

In conclusion, propofol given by repeat bolus or continuous infusion produced good anaesthetic conditions. In this study we were unable to demonstrate any clear advantage of a continuous infusion technique over a conventional repeat bolus technique. The infusion technique may prove useful for longer day case procedures such as laparoscopy, arthroscopy and dental extractions.

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The role of the teaching hospital

A survey of paediatric anaesthetic techniques used by trainee anaesthetists on a regional training scheme

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Summary

All trainee anaesthetists on the Northern Ireland training scheme were surveyed about the techniques they use when anaesthetising elective paediatric cases. We compared the practice of doctors with specialist paediatric training to that of others and discovered that trainees with specialist training were more likely ($p < 0.05$) to admit parents during induction, but were less likely ($p < 0.05$) to visit their patients pre-operatively and routinely to use suxamethonium. Other general findings were confusion over the re-use of halothane and extensive involvement of trainee anaesthetists in neonatal resuscitation.

Key words

Anaesthesia; audit, paediatric.

All trainee anaesthetists give anaesthetics to children, usually for routine elective surgical cases. Little data exist on the quality of care that trainees provide for these young patients or the anaesthetic training they receive.

Our aim was to collect information on the techniques employed in elective paediatric anaesthesia by anaesthetists below consultant grade in the Northern Ireland training scheme. We also investigated the effect that experience in

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the regional specialist paediatric surgical unit has on this practice.

Methods

All trainee anaesthetists working in Northern Ireland received a questionnaire about routine elective anaesthesia of healthy children aged between 1 and 14 years. Trainees were asked to answer according to their own personal practice when not supervised by a consultant. We considered emergency work too heterogeneous a subject for a short questionnaire. The replies were separated into two groups for comparison: group 1, all juniors with experience of working in the regional children's hospital; group 2, all other trainees undertaking unsupervised paediatric anaesthesia.

Most of the trainees in group 1 were senior registrars. To reduce any error which may have arisen from the comparison of the practice of more generally experienced senior registrars with that of the more junior trainees we disregarded the replies of trainees with less than 3 years experience. Therefore we restricted group 2 to experienced senior house officers (SHOS) and registrars. The responses of the two groups were tabulated and compared using Fisher's exact probability test.

Results

The survey produced 56 replies, an 80% response. The replies were from 15 senior house officers, 18 registrars and 19 senior registrars. All of the senior registrars and five of the registrars but none of the SHOs had worked at the regional children's hospital. When the replies were divided as outlined above there were 20 doctors in group 1 and 21 in group 2.

The effects of experience of the regional children's hospital (Table 1). Doctors with experience of the regional children's hospital were significantly more likely to admit parents to the anaesthetic room ($p = 0.043$). They alone employed spinal, intercostal and brachial blocks in children. On the other hand, they were less likely to visit their patients before operation and to premedicate them ($p = 0.03$). Doctors in group 1 also use suxamethonium for routine intubation significantly less frequently than those in group 2 ($p = 0.024$). In answer to all other questions the replies of the two groups did not differ.

Pre-operative care. All respondents expect children to be weighed and calculate drug and fluid requirements accordingly. Only seven (33%) doctors in group 1 always visit their patients before operation, compared with 16 (80%) in group 2. There were no significant differences between groups in the premedications used. EMLA cream is the most popular drug, used routinely by 93% of juniors. Other premedications used are, trimiprazine syrup (54%), oral diazepam (21%) and intramuscular pethidine/atropine (8%). Eleven (21%) use no premedication.

Induction of anaesthesia. Group 1 trainees were significantly more likely to admit parents during induction than those in group 2, (62% as opposed to 35%). Suxamethonium is preferred to the nondepolarising relaxants for the intubation of elective cases by those in group 2 (90%), whereas only 57% of trainees in group 1 expressed this preference. There was no significant variation between groups in the preferred method of induction of anaesthesia. Intravenous induction is the most popular method, used by 86%; inhalational induction (invariably with halothane) is used by 7.6%, and 5.7% stated no preferred method.

Regional techniques. Five doctors in group 1 (24%) use spinal, intercostal and brachial plexus blocks in children. None of those in group 2 use these. Other regional blocks are employed equally frequently by both groups (always in combination with general anaesthesia). The overall percentages using each technique were: caudal (81%), dorsal penile (75%), wound infiltration (65%), and illio-inguinal field block (60%).

In all subsequent responses there were no significant differences between groups 1 and 2. The figures given below refer to both groups added together.

Maintenance of anaesthesia. Isoflurane is the most popular maintenance volatile agent (used by 26 (50%)). Halothane is preferred by 23 (44%) and three (6%) routinely use enflurane. Fifty-seven percent of respondents considered that it was safe to repeat halothane anaesthesia in children, but there was a wide variation in the interval they considered acceptable between exposures to this drug. Twenty percent consider 3 months to be safe, 56% allow 6 months and 34% allow at least 1 year.

Preferred monitors. Trainees were asked to list the forms of intra-operative monitoring they regard as essential. The results were as follows; ECG (96%), pulse oximeter (92%), noninvasive blood pressure (85%), praecordial stethescope (53%), end-tidal CO_2 (18%) and temperature (15%).

Non anaesthetic work in the labour ward. Most (70%), have experience of obstetric anaesthesia, and of these 94% have been asked by paediatricians to assist with neonatal resuscitation. These requests always occurred during emergency Caesarean sections. Anaesthetists were asked to intubate the neonate (94%), to supervise the paediatrician (4%) and to obtain venous access (2%). Sixty-nine per cent of trainees answering this section have had training in neonatal resuscitation.

Discussion

In Northern Ireland the Royal Belfast Hospital for Sick Children is the only specialist unit catering for neonatal surgery, most major paediatric surgery and paediatric intensive care. The other teaching and district general hospitals undertake some emergency neonatal surgery and many minor and intermediate paediatric procedures with a large day care component. All trainees are centrally appointed and usually rotate through a different hospital each year.

Table 1. The effect of experience in the regional children's hospital (significantly different practices).

	Group 1 (With experience)	Group 2 (No experience)
Visiting patients before operation	7 (33%)	16 (80%)
Premedicating	12 (57%)	19 (95%)
Admitting parents	13 (62%)	7 (35%)
Using suxamethonium	12 (57%)	19 (90%)
Using spinal, intercostal and brachial plexus blocks	5 (24%)	0 (0%)

We compared the practice of doctors who have worked in the regional children's hospital with those who had not done so, but who had at least 3 years' anaesthetic experience. The latter group were significantly more likely to visit their patients before operation and to premedicate them. Oral premedication seems to have displaced parenteral premedication. The most popular single premedication is EMLA cream, now used by nearly all trainees. This effective drug has made intravenous induction more acceptable and may explain the 86% preference for intravenous rather than gaseous induction.[1] Intravenous induction is now much less traumatic than it used to be, so it is disappointing that only 35% of those trainees without specialist training permit parental presence at induction of anaesthesia. Parental presence has been associated with smoother induction and reduced anxiety for both patients and parents.[2] Reassuringly, 62% of the specialist trained anaesthetists admit parents during induction.

Ninety percent of the doctors without experience of the children's hospital use suxamethonium for routine elective intubation. This may be undesirable in view of evidence that suxamethonium is a trigger of malignant hyperthermia and may cause life threatening arrythmias in apparently healthy children as well as unpleasant peri-operative dreaming.[3,4] The percentage using suxamethonium in this fashion falls to 57% in the group with specialist training.

Spinal, femoral, sciatic and intercostal nerve blocks have been used under general anaesthesia in children for postoperative pain relief.[5–7] However, in this survey only five senior registrars with specialist training use these techniques.

Perhaps these differences, considered together, reflect a lack of confidence, the doctors without specialist training preferring a well sedated patient with a rapid induction and intubation ideally without an onlooking parent. In this study isoflurane and halothane were almost equally popular as maintenance agents. Halothane is the volatile agent used for gas inductions. Evidently there is confusion about the re-use of halothane and the interval that should be allowed between exposures. The majority of respondents use regional anaesthetic techniques where possible, especially caudal and dorsal penile blocks though not spinal, brachial plexus or intercostal blocks (Table 1). This may be related to the increase in day surgery for which the popular technique of general anaesthesia and regional block are well suited.[8] The third most popular technique is local wound infiltration which is effective and easily performed.[9] The ECG is the most common monitor, closely followed by the pulse oximeter. The sphygomonometer and precordial stethoscope are much less popular. Perhaps in the practice of these doctors the pulse oximeter has displaced the praecordial stethoscope as the 'beat to beat' monitor during paediatric anaesthesia. End-tidal CO_2 monitoring is unpopular, coming low on the list of preferred monitors. This is unfortunate because the capnograph is an effective early detector of respiratory obstruction, disconnection and malignant hyperpyrexia.[10,11] This is especially relevant since most trainees do not consider a temperature probe as preferred monitor.

In the labour ward nearly all these anaesthetists had been asked for help with neonatal resuscitation although many of them have had no training in neonatal resuscitation. As all of these requests occur during emergency Caesarean section when the anaesthetist is usually single handed, he or she cannot be adequately observing the mother during this critical stage of the operation.

In conclusion, we suggest that this survey shows that apart from teaching specialist techniques paediatric anaesthetic training makes junior doctors more confident in their management of children. Most of the anaesthetists returning our questionnaire use similar and theoretically sound techniques. Practice could be improved by promoting parental presence at induction, reducing the routine use of suxamethonium and encouraging more end-tidal CO_2 monitoring. Evidently more widespread training in neonatal resuscitation and a policy on when to repeat halothane in children are also required.

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Comparison of two techniques for sedation in dental surgery

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Summary

Forty-eight patients were randomised to receive sedation for outpatient dental surgery with midazolam. Sedation was given using the Verrill technique (24 patients) and the Glasgow Dental Hospital technique (24 patients). The differences in recovery and patient acceptability were assessed. There was no statistical difference in mean recovery times between the two groups. Memory function was examined using the Warrington memory test. Fewer patients in the Verrill group recalled the injection of local anaesthetic but they demonstrated memory defects 4 hours after sedation for words and 3 hours for faces. The Glasgow Dental Hospital group demonstrated memory defects for words up to 2 hours following sedation, but not for faces at any time. Thirty-eight patients would have dental surgery again with similar sedation. The dental surgeon found conditions for surgery inadequate in two patients. In view of the shorter duration of amnesia we recommend the Glasgow Dental Hospital technique.

Key words

Hypnotics, benzodiazepines; midazolam.
Surgery; dental.

Midazolam has proved to be a reliable and safe method for intravenous sedation in dental outpatients.[1] There are two different techniques of midazolam sedation currently in use. The Verrill technique, where the end-point is ptosis[2] and the technique used in the Glasgow Dental Hospital (GDH) where sedation is considered satisfactory when the patient becomes less responsive on direct questioning.[3]

In their study, Skelly and colleagues[1] used the Verrill technique and showed a significant memory impairment at 5 hours with midazolam given at a mean dose of 12.73 mg (range 5–18 mg). They concluded that instructions should warn of continuing impairment. A recent study by Ho and colleagues[4] comparing midazolam and isoflurane in dental sedation has also shown a significant impairment of memory one hour postoperatively in the midazolam group despite the use of a smaller dose of midazolam, 5.5 mg (range 3–10 mg).

The aim of this study was to compare the two different techniques of midazolam sedation to determine any difference in amnesia, in the rate of recovery, or in the patients' opinions.

Patients and methods

Approval was granted by the local Ethics Committee. We studied 48 patients, aged 16–60 years, who required minor dental surgery under sedation. Patients were excluded if they were not ASA 1 or 2, if they took any psychotropic medication, or were pregnant. The study was observer and patient blind. Patients were allocated randomly to receive sedation by the GDH or Verrill techniques. Informed consent was obtained from all patients.

The memory test developed by Warrington was used as described in the previous study by Ho and colleagues[4] but with the addition of two further sets each of 25 words and faces. Patients were tested before sedation to obtain a baseline score, and then 2, 3 and 4 hours following administration of midazolam. The order of the sets of memory tests was randomised to prevent any bias.

Anxiety was assessed by the Corah dental anxiety scale[5] and a visual analogue scale (VAS). Systolic arterial pressure, heart rate and oxygen saturation ($Sa{O_2}$) were measured during the procedure using an automated system consisting of an Ohmeda Biox 3700 pulse oximeter and a Critikon Dinamap 1846 noninvasive arterial pressure monitor. These were interfaced to an Atari 1040 ST microcomputer programmed to store data on magnetic disc at 2-minute intervals.

In the dental chair a 23-gauge cannula was inserted in the back of the hand. The Verrill group received 2 mg midazolam then intermittent doses of 1 mg/minute up to a maximum of 10 mg. The end-point was taken as the degree of ptosis demonstrated when the eyelid was halfway across the pupil, unless the patient previously showed excessive drowsiness, slurred speech or nystagmus. The GDH group received 2 mg midazolam, then intermittent doses of 1 mg/minute up to 5 mg, then 0.5 mg/minute up to 10 mg. The end-point was judged by the patient's loss of interest in maintaining conversation, with a tendency to monosyllabic replies rather than extended sentences. The patient no longer directed his gaze to the speaker and tended to forget the trend of conversation. The duration of blinking lengthened and there was a loss of tone in the arm. The anaesthetist who sedated all the patients (G.D.P.) was the only investigator aware which method of sedation was used in each case, and he was not involved in testing recovery from sedation or testing memory function. The dental surgeon injected local anaesthetic, lignocaine 2% with adrenaline. Recovery tests, as in the previous study,[4] were performed 10 minutes after the end of the procedure, and every subsequent 5 minutes until the patients were capable of walking unaided in a straight line. The patients were

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discharged 4 hours after surgery with written and verbal postoperative instructions. They returned a questionnaire when they visited the dental surgeon one week later.

Results

Forty-eight patients were studied, seven males and 17 females in the Verrill group, and two males and 22 females in the GDH group. Forty patients had extraction of teeth, one an exploration, two curettage, four apicectomies, and one had excision of a lesion of the hard palate.

There was no statistical difference in the age or weight of the two groups (Table 1). Corah dental anxiety scores were similar in both groups. Postoperatively there was a significant decrease in VAS for anxiety in both groups, but there was no significant difference between the groups. The patient estimated the duration of surgery to be less than the true value. Durations of surgery were similar, as were the times to injection of local anaesthetic. The mean dose of midazolam administered in the Verrill group was 8.18 mg (range 5–10 mg) and 5.4 mg (range 3–10 mg) in the GDH group, and the difference of the means did not reach full significance ($p < 0.1$, Mann–Whitney *U* test). Ptosis, as in the Verrill technique with the eyelids half over the pupil, was not seen in any patient in the GDH group. Full ptosis was only achieved in the Verrill group in nine out of the 24 patients; excess sedation with diplopia and drowsiness was seen. The mean recovery time in the Verrill group was 21.5 (range 10–35) minutes. This was not statistically significant from the mean recovery times in the GDH group, 16.9 minutes (range 10–25 minutes), (Table 1).

There was no significant difference between the lowest $Sa\text{O}_2$ recorded during the procedure in the two groups. In the Verrill group, the lowest value recorded was 89%, (mean 93.8, range 89–99), and in the GDH group the lowest value was 91% (mean 94.6, range 91–98). There was a significant increase from baseline values in systolic arterial blood pressure at the end of the procedure, ($p < 0.0001$), but no statistical difference between the two groups. In the Verrill group, the increase in heart rate was statistically significant, ($p < 0.05$), but there was no significant change in the GDH group (Table 2).

The dental surgeon rated surgical conditions as satisfactory in 46 patients. One patient became very weepy and not fully cooperative and sedation was judged inadequate. The technique was a failure in another patient; he remained anxious and uncooperative during surgery. Both patients were in the Verrill group.

The patients were questioned at the end of surgery to assess their opinion of the sedation. Significantly more patients recalled the injection of local anaesthetic in the GDH group compared to the Verrill group (Table 3). There was no statistical significance between groups in recall of the procedure (Table 3). In the Verrill group, six patients felt they still had some degree of anxiety during the operation, while four patients acknowledged anxiety in the GDH group. Only two patients experienced dreams. One patient in the GDH group could not recall the content of the dream. The second patient, in the Verrill group, dreamed of a previous unpleasant dental experience. This patient was judged to have been inadequately sedated by the dental surgeon. On specific questionning 7 hours after sedation she did not recall the dream.

Memory Tests. The results of the memory tests are illustrated in Figure 1. There was no significant difference between groups for the baseline retention scores assessed before operation for words and faces. In the Verrill group the falls in retention scores for words were significant at 2 and 3 hours ($p < 0.001$ in each case; Wilcoxon signed rank test, Bonferroni correction) and also at 4 hours ($p < 0.05$; Wilcoxon signed rank test, Bonferroni correction). In the GDH group, the decreases in retention scores for words was only significant at 2 hours ($p < 0.01$, Wilcoxon signed rank, Bonferonni correction). For faces, significant falls in the retention scores were seen in the Verrill group up to 3 hours ($p < 0.01$ in each case; Wilcoxon rank test, Bonferroni correction). In the GDH group the decreases in the retention scores were not statistically significant.

Patient Questionnaire. Eighty-nine percent (22/24) in the Verrill group and 85% (21/24) in the GDH group returned questionnaires (Table 4). There was no significant difference between the two groups. A similar incidence of side

Table 1. Demographic data and operative details, (mean (SD)).

	Verrill group	GDH group
Number of patients	24	24
Age; years	23.67 (5.6)	27.08 (11.93)
Weight; kg	64.73 (14.42)	62.98 (10.52)
Corah dental scale	11.08 (0.76)	11.38 (0.72)
Anxiety VAS; cm		
Before operation	5.36 (2.34)	5.10 (2.60)
After operation	0.92 (0.76)	1.44 (1.70)
Duration of operation; minutes	32.96 (12.16)	30.21 (13.83)
Time to injection of LA	8.58 (0.43)	6.29 (0.40)
Recovery time; minutes	21.46 (6.84)	16.88 (10.85)
Midazolam dose; mg	8.19 (1.92)	5.4 (1.80)

VAS, visual analogue scale; LA, local anaesthesia.

Table 2. Systolic arterial pressure (mmHg).

	Verrill group	GDH group
Before surgery	116.04 (15.23)	109.46 (11.08)
After surgery	131.75 (18.43)	127.67 (16.54)
	Heart rate	
Before surgery	72 (12)	75.79 (13.4)
After surgery	80 (13.4)	77 (13.2)

Table 3. Patients' assessment of sedation.

	Verril group	GDH group
Number of patients	24	24
Estimation of mean duration of the procedure; minutes	22.88	19.88
Remembered		
Injections of LA	5	15*
Dental procedure	11	18
Opion of LA (if remembered)		
Acceptable	4	13
Unpleasant	1	0
Painful	0	2
General opinion		
Anxious	6	4
Comfortable/relaxed	18	20
Dreams	1	1
Would have the same again	23	21

LA, local anaesthesia. *$p < 0.01$; Chi-squared with Yates' correction.

Table 4. Postoperative side effects (number of patients).

	Verrill group (n = 22)		GDH group (n = 21)	
	Evening	Next day	Evening	Next day
Drowsiness	14	8	15	4
Lack of ability to concentrate	13	5	11	5
Dizziness/unsteady	8	6	6	4
Nausea	3	3	5	5
Vomiting	2	0	2	2
Headache	8	7	9	9
Muscle pain/stiffness	6	6	3	1
Pain at site of dental procedure	17	14	13	12
Pain at site of injection in the hand	4	3	3	2
Sore throat	5	4	6	6
Time to return to work				
Next day	7		6	
Later	15		15	
Would have same sedation again	18		18	

effects was recorded by both groups; over 50% felt drowsy, were unable to concentrate and had pain at the operation site the same day. Thirty out of the 41 patients who returned the questionnaire had not returned to work the next day. Thirty-eight patients said they would like a similar sedation technique if they required further surgery.

Discussion

Sedation techniques are now commonly used in outpatient dental chair surgery. The benzodiazepine midazolam is a suitable alternative to diazepam in outpatients because of its short half-life and inactive metabolites.[6] Its amnesic properties are well documented.[7,8] This is important during the surgical procedure but gives some cause for concern in day case patients who may forget instructions issued to them at the time of discharge from the dental surgery. The Warrington memory test was used by Ho and colleagues[4] to assess memory function after intravenous midazolam and inhalation of isoflurane, and they found the test to be reliable and easy to use, as we did. Simple recognition of words and faces is 'patient friendly'. Memory impairment is dependent on the dose of benzodiazepine[9] and as a previous study[1] using the Verrill technique appeared to have used a higher dose than the alternative technique it seemed possible that there would be more amnesia after the use of the Verrill technique. In our study the difference in dosage between the two groups did not achieve full significance, even though in the Verrill technique the patient was titrated to a deeper degree of sedation, with marked ptosis. The lack of significance in the mean dosage was, we believed, related to the wide range of doses required in the individual patients.

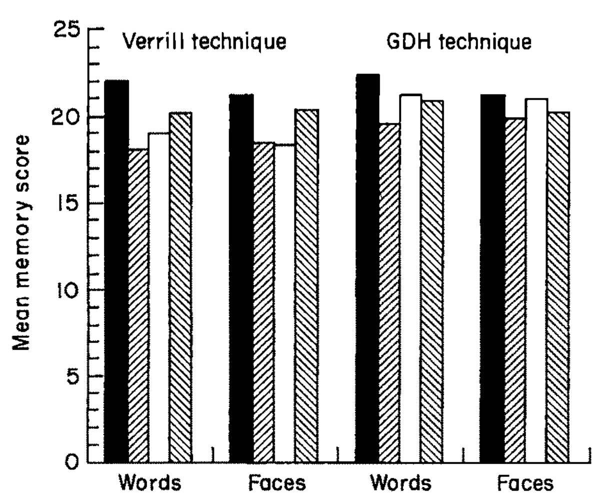

Fig. 1. Mean memory score for words and faces before and after sedation. There was a significant reduction in mean scores in the Verrill group for words at 2 and 3 hours ($p < 0.001$) and also at 4 hours ($p < 0.05$). For faces the reduction in scores was significant at 2 and 3 hours ($p < 0.01$). There was a significant reduction in scores for words in the GDH group up to 2 hours after sedation ($p < 0.05$). The reduction in scores for faces in the GDH group was not significant. (Wilcoxon signed rank test, Bonferroni correction). ■, 0 hours; ▧, 2 hours; □, 3 hours; ▨, 4 hours.

The deeper degree of sedation with the Verrill technique was associated with significantly greater amnesia for the local anaesthetic injections. Defects in memory, as shown by the Warrington memory tests, were seen up to 4 hours after the Verrill and 2 hours after the GDH technique. Our results are in keeping with those of Skelly and her colleagues[1] who also demonstrated amnesia at 5 hours after the Verrill technique, using a larger dose of midazolam.

Both techniques gave comparable results apart from the differences in the memory tests. There were no significant differences in recovery times, dental surgeon or patient opinions or in the longer term side effects reported on the questionnaire. Comparable numbers of patients in each group reported willingness to be sedated in a similar manner again for dental surgery. Some patients considered sedation was an unnecessary adjunct to local anaesthesia for them personally and would therefore decline sedation again. One patient who requested a general anaesthetic before being offered sedation would still have preferred general anaesthesia when questioned at the end of the procedure. This same patient was judged inadequately sedated by the dental surgeon, and possibly came to the surgery with preconceived ideas about sedation for dental surgery. Dreaming in the dental chair while having surgery under sedation is reported[10] and may result in litigation.[11] In this study only two patients reported dreams during the procedure. This may be related to the lower doses used in this study.

In conclusion, memory defects were demonstrated for up to 4 hours after use of the Verrill technique and at 2 hours using the GDH technique. The Verrill technique also gave more amnesia for the injection of local anaesthetic, but the GDH technique may be preferred since it produces less memory defect during the hours following the surgery. In view of the memory defects with both techniques we would recommend written instructions are given to the patient before sedation and also, at discharge, to the patient's escort. We would also recommend that dentists are instructed in the use of the GDH technique by anaesthetists teaching sedation for dental surgery.

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Haemodynamic effects of propofol in children

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Summary

The haemodynamic effects of induction of anaesthesia with propofol in children were studied. Two hundred and sixteen children (ASA 1) were randomly allocated to receive one of six different doses of propofol, from 1.6 mg/kg to 2.6 mg/kg, in 0.2 mg/kg increments. Noninvasive measurement of blood pressure showed that mean arterial pressure was reduced by approximately 15% after 1 minute, and by 30% after 5 minutes. The reduction in pulse rate over a 5-minute period was approximately 17%. These changes were similar in each group, regardless of the dose administered. The propofol was mixed with lignocaine, 0.5 mg/ml, and the incidence of pain on injection into a vein on the dorsum of the hand was 24%. We conclude that, within the dose range of our study, the haemodynamic disturbance after induction of anaesthesia with propofol in children is not dose related.

Key words

Anaesthetics, intravenous; propofol.
Anaesthesia; paediatric.

Propofol has become increasingly popular as an induction agent since its introduction in 1983. This is primarily due to rapid recovery conferred by its high plasma clearance and short half-life.[1] In common with many intravenous induction agents, it causes a decrease in blood pressure on induction of anaesthesia. The reduction in blood pressure with propofol is observed to be more than that with thiopentone in both adults[2] and children.[3] Studies in children suggest that they require a larger induction dose of propofol than adults, probably in excess of 2.5 mg/kg.[3,4] However, larger doses of propofol may be associated with pronounced haemodynamic side effects.[5] The aim of this study was to determine whether or not there was a dose-related change in haemodynamics following induction of anaesthesia with propofol in children.

Method

Approval for this study, and for the use of propofol in children, was granted by the Chinese University Research Ethics Committee and informed parental consent was obtained. Two hundred and sixteen children (ASA 1),

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between 8 months and 12 years of age who were scheduled for minor surgery, were studied.

A stratified random allocation was used to divide the children into six dose groups. These were propofol 1.6, 1.8, 2.0, 2.2, 2.4, or 2.6 mg/kg.

All children had EMLA cream applied to the dorsum of both hands which were then covered with an impervious dressing, approximately one hour before the estimated time of anaesthesia. No other premedicant was given.

On arrival in the anaesthetic room, a noninvasive automatic blood pressure monitor (Dinamap 845XT Critikon Ltd.) was applied to one arm and a 24-gauge cannula was inserted intravenously into the other hand, where an oximeter probe was attached for monitoring the oxygen saturation. The child was allowed to settle and a baseline blood pressure reading was taken. Following this, the predetermined dose of propofol was given over a period of approximately 20 seconds. One percent lignocaine 0.05 ml was added to each millilitre of propofol immediately before administration. The Dinamap was set to monitor and record at one minute intervals. As soon as the child would tolerate it, a facemask was gently applied and the patient was allowed to breathe spontaneously a mixture of nitrous oxide 30% and halothane 0.5% in oxygen through a modified Ayre's T-piece. The child was not disturbed during the study period of 5 minutes, to avoid producing haemodynamic changes.

Pain on injection was assessed by the reaction of the child during administration of the drug. In older children, spontaneous complaint of pain or a withdrawal response was used to indicate pain. For children under 3 years of age, grimacing, a cry on induction, or a withdrawal response was used instead. The attitude (anxious or calm) of the patient before induction was also noted.

A multivariate analysis of variance for repeated measures was used to analyse the demographic data, blood pressure, and pulse rate changes. A p value of < 0.05 was considered to be statistically significant.

Results

The demographic details of the patients are shown in Table 1. There was no statistically significant differences between the age, weight, and sex of the children in any of the dose groups, nor was there any significant difference in the pre-operative blood pressures and pulse rates between the dose groups.

The mean values of systolic, mean arterial and diastolic blood pressures decreased significantly following induction in all six groups, $p < 0.001$. Figure 1 shows the changes in mean arterial pressure for each group over 5 minutes following induction. The reduction in mean arterial pressure over the first minute was approximately 15% and after 5 minutes approximately 30%. However, there was no difference between the six dose groups at any given time (between-group effect). p values were 0.3, 0.6, and 0.9 for systolic, mean, and diastolic arterial pressures respectively. There was also no significant difference in the rates of decline of blood pressure between the dose groups (group-

Table 1. Demographic data.

Propofol dose (mg/kg)	1.6	1.8	2.0	2.2	2.4	2.6
n	34	34	38	35	42	33
Age (years) mean	5.74	5.56	5.26	5.23	5.00	4.94
SEM	0.59	0.59	0.52	0.54	0.51	0.55
Weight (kg) mean	21.7	20.3	19.3	19.7	18.6	19.7
SEM	1.77	1.58	1.29	1.50	1.21	1.35
Sex (M/F)	29/5	32/2	28/10	27/8	29/13	26/7

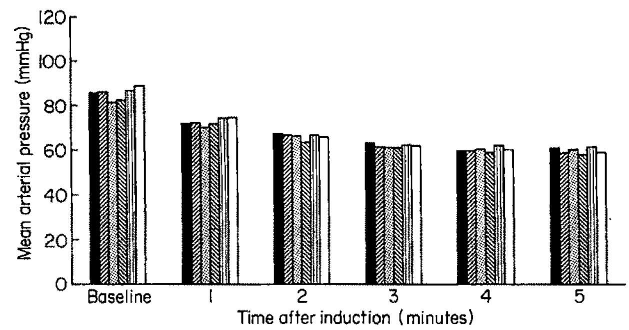

Fig. 1. Changes in mean arterial pressure (mmHg) following propofol. Mean values for each dose group: ■, 1.6 mg/kg; ▨, 1.8 mg/kg; ▤, 2.0 mg/kg; ▧, 2.2 mg/kg; ▥, 2.4 mg/kg; □, 2.6 mg/kg.

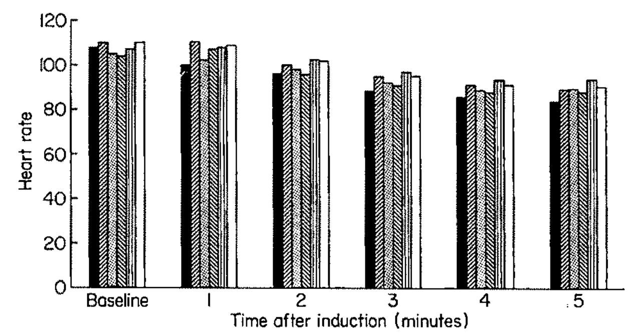

Fig. 2. Changes in heart rate following propofol. Mean values for each dose: ■, 1.6 mg/kg; ▨, 1.8 mg/kg; ▤, 2.0 mg/kg; ▧, 2.2 mg/kg; ▥, 2.4 mg/kg; □, 2.6 mg/kg.

time interaction). p values were 0.8, 0.8, and 1.0 for systolic, mean, and diastolic arterial pressures respectively.

Analysis of pulse rate changes shows a similar trend to that of the blood pressures (Fig. 2). There was a significant reduction in pulse rate of approximately 17% over the 5 minutes following induction, although there was no differences between dose groups ($p = 0.5$ for between-group effect, 0.7 for group-time interaction).

The incidence of pain on injection was 24.1%, and 34.9% of children appeared anxious before induction. There was no significant difference in the incidence of pain or anxiety between the dose groups.

Discussion

Our results show that the reductions in blood pressure and pulse rate following propofol induction in children are not dose related. This is different from the findings of Major *et al.*,[5] who demonstrated a dose-related decrease in arterial pressure and increase in heart rate in adult females. The dose range we used was similar to theirs, although our patients were divided into six dose groups within the range rather than three. Their work was undertaken using the old formulation of propofol in Cremophor, whereas we used the new emulsion formulation. However, the difference in results is unlikely to be attributable to the use of different preparations, as Glen and Hunter have shown similar anaesthetic and haemodynamic effects with both formulations.[6]

Propofol consistently produces a greater decrease in blood pressure than other agents such as thiopentone,[2,7,8] and methohexitone.[9] Several mechanisms have been suggested to account for hypotension following propofol.

Claeys and colleagues,[10] in an adult study, suggested that a decrease in afterload is the principal mechanism. Goodchild and Serrao,[11] in animal experiments, concluded that it is because of a decrease in cardiac output secondary to reduced preload; the latter was due to vasodilatation of capacitanee vessels caused by a direct effect of propofol, and the decrease in sympathetic tone following loss of consciousness. Invasive cardiovascular monitoring was not performed on ethical grounds, so the exact mechanism of hypotension in our paediatric patients is unknown, although it is likely to be similar to that in adults.

We demonstrated a decrease in pulse rate which was unrelated to dose. This appeared to be greater than that demonstrated in some adult studies in which there was a modest decrease or no decrease in heart rate after induction.[2,7,10,12] In contrast, Major *et al.*[5] showed a dose-related initial increase in heart rate. They suggested that this may be the result of pain on injection which occurred in 80% when propofol was administered via a vein on the dorsum of the hand. Our findings show no early tachycardia, perhaps because of the low incidence of pain (24%) associated with the addition of lignocaine. The fact that our children had a more profound decrease in heart rate may be due to their higher resting vagal tone.

The use of inhalational agents during the study (nitrous oxide and halothane) may be criticised, since both of these agents produce haemodynamic effects. However, our results obtained whilst using inhalational agents may reflect more accurately haemodynamic changes which occur in clinical practice.

As propofol produces an unacceptably high incidence of pain on intravenous injection, lignocaine 10 mg was added to each 20 ml ampoule of propofol immediately before injection, as previously recommended by Brooker and Redfern.[13] However, subsequent investigations of this problem have produced conflicting conclusions. In Morton's study, the addition of lignocaine failed to improve pain on injection,[14] whereas Helbo-Hansen and colleagues[15] showed that there was a reduction in pain from 32.5% to 5% with the use of lignocaine. Patel and colleagues[4] found the incidence of pain with lignocaine addition to be 27%. This is comparable to our figure of 24.1%, although only 7.0% of our patients experienced severe pain.

We conclude that in children induction of anaesthesia with propofol produces a decrease in blood pressure and pulse rate similar to that seen in adults. However, unlike adults, the changes are not dose related. The degree of hypotension produced would not be hazardous in most children. However, for those in whom haemodynamic disturbance should be avoided, modification of the induction technique may be considered. This might involve a slower rate of administration of propofol or pretreatment with a vagolytic agent such as atropine. Further investigation is required to evaluate the merit of such methods.

Acknowledgments

We are grateful to Mr J. Lau of the Centre for Clinical Trials and Epidemiological Research at the Chinese University of Hong Kong for his assistance with the statistical analysis.

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Anaesthesia, 1991, Volume 46, pages 786–803

Correspondence

Variables of patient-controlled analgesia

The study of Owen *et al.* (*Anaesthesia* 1990, **45:** 619–22) concluded that there was a significant linear trend to increasing amount of demand morphine with increasing bolus size when patient controlled analgesia (PCA) was used following gynaecological surgery. The implication is that patients do not titrate themselves to an appropriate plasma level of opioid for relief of postoperative pain, but rather that they demand boluses at a rate which has little to do with the amount of opioid received. This conclusion, if correct, is of importance in the interpretation of studies which utilise PCA to quantify the efficacy of analgesics; in fact it undermines the whole rationale of such studies.

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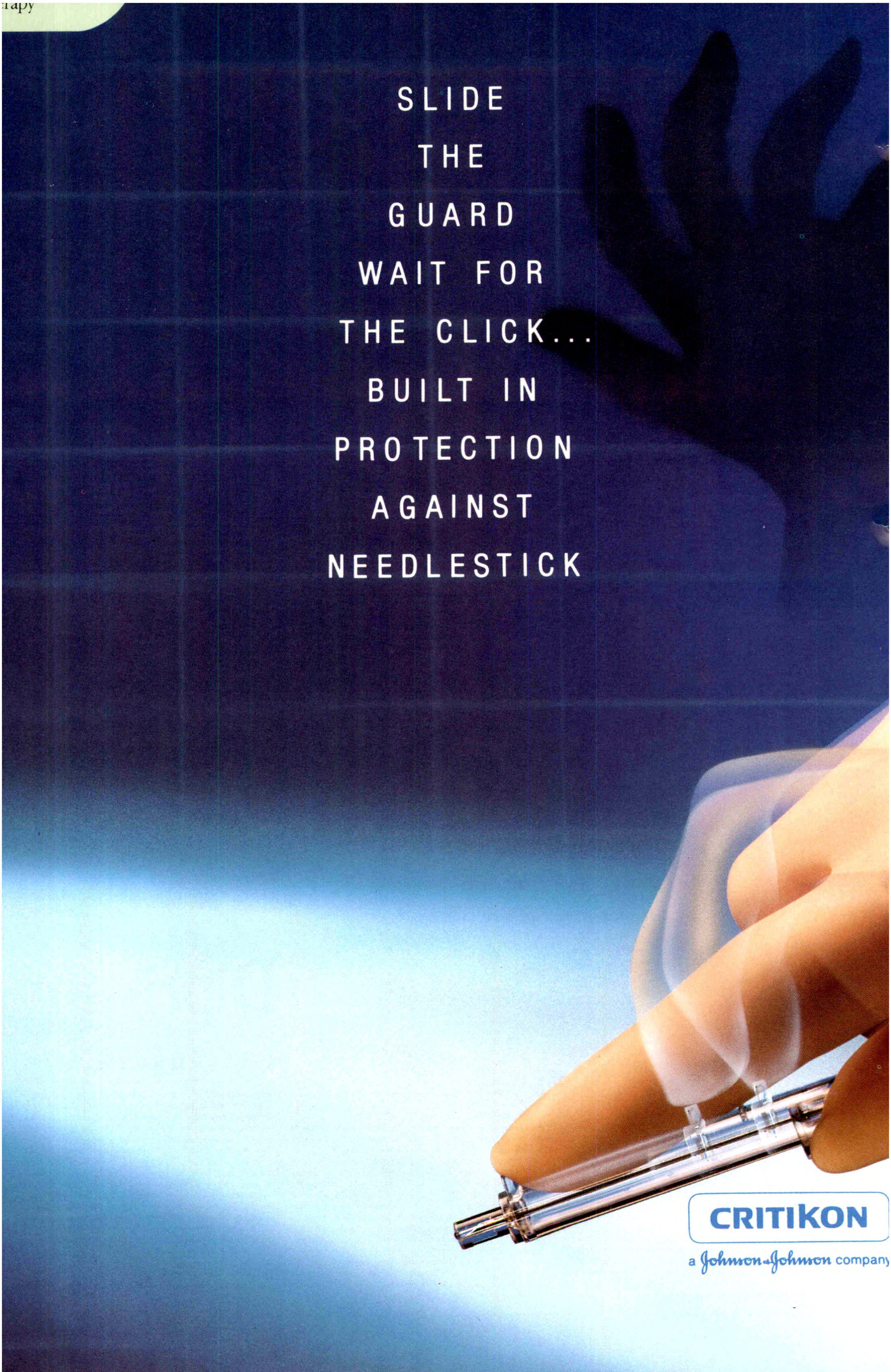


Clinical issues in agent vaporization technology.

New clinical techniques and vaporizer technologies now make volatile anaesthetic agent delivery more predictable and much safer. However, older vaporizers remain in use and, while sometimes offering features anaesthetists may still find desirable, they may not be equipped with key features that are available on today's units.

The debate—use of older vaporizers versus newer units—centres on several clinical issues:

- **Adverse patient reactions** can be greatly reduced by combinations of current vaporizer technologies, including: *interlocking* to help prevent activation of multiple units and delivery of agent "cocktails;" *keyed filling* to help assure filling of vaporizers with the proper agent; and *circuit isolation* to protect the gas stream from trace agent contamination. Together, these systems address hypotension, bradycardia, prolonged emergence, cardiac arrest[1] malignant hyperthermia and halothane hepatitis caused by unintended agent delivery.

  Malignant hyperthermia is a pharmacogenetic complication of anaesthesia[2] with relaxants and inhalation anaesthetics[3] Though rare, it remains a cause of anaesthetic-induced death[4] It has been reported that trace agent delivered by vaporizers not fully isolated from the gas stream when "off" has initiated malignant hyperthermia in a susceptible patient[5]

  Halothane hepatitis is also related to agent delivery. The minimum initiating dosage is not known, nor is there clear indication whether it is dose- or threshold-limited[6] As with malignant hyperthermia, trace halothane may present a hazard to susceptible patients, and isolation of the vaporizer from the gas stream is recommended[7]

- **Dosage specificity** is enhanced, in part, by vaporizer keyed filling that helps ensure that a vaporizer is filled with the proper agent. Coupled with vaporizer interlocking, vaporizer agent-specificity and enhanced vaporizer labelling, keyed filling helps protect against delivery of an unplanned mixture.

- **Environmental issues**—especially the growing concern about the long-term effect of agent on the surgical staff—are addressed through a variety of means associated with vaporizers:

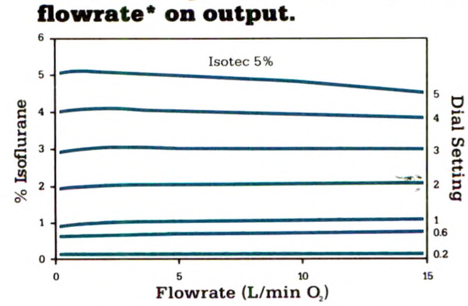
  Keyed filling: Data are inconclusive, but studies point to keyed ports as a way to reduce pollution during filling[8] especially compared to the spillage possible with funnel-fillers.

  Vaporizer mounting: Demountable vaporizers allow removal for filling outside the operating theatre, under a fume hood or in an area with greater ventilation than the operating theatre.

  Vaporizer venting: Some vaporizers vent excess pressurized agent to the atmosphere, increasing its concentration in the operating theatre. Current designs like the Tec 5 do not require such pressure and agent venting.

- **Dosage accuracy** is enhanced by modern vaporizers which are designed to deliver consistent and predictable concentrations regardless of flow, carrier gas composition, temperature, atmospheric pressure and backpressure from downstream components.

Performance characteristics of the Tec 5 Vaporizer: The effect of flowrate* on output.



*At 22°C with oxygen flowing. Performance is similar with enflurane and halothane models.

Accuracy is also affected by control system performance, with units now offering more finite control. Advance technology allows delivery verification through sophisticated agent monitoring.

- **Operational issues** have their greatest impact on the clinician as they affect equipment service, equipment utilization and, ultimatel anaesthesia department budgets. Newer vaporizers, with their extended service and warranty plan help reduce budget and downtime. These units can be quickly interchanged on the anaesthesia machine allowing the anaesthetist to change agent combinations as needed.

For more information on these important clinical issues, and others involved in volatile anaesthetic agent vaporization, please consult an Ohmeda representative.

Ohmeda.
A world of choice in anaesthesia

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However, I am not convinced that the illustrated data necessarily support the conclusion. The same authors have already demonstrated that patients receiving a PCA bolus of 0.5 mg morphine were frequently unable to achieve good pain control, and suggested then that there may be a self-imposed maximum demand rate which patients are reluctant to exceed.[1] If it is allowed that the 0.4 mg dose was inappropriately small (even with the addition of the low dose infusion), and the results of the 0.7 mg and 1.0 mg groups are examined on their own, it appears that the morphine consumption of patients in these two groups were remarkably similar (in Figure 2 their graphs of cumulative morphine dosage virtually overlap). This similarity is enhanced if the dose given by infusion is included (as, surely, it logically should be); by deduction from the presented data, the cumulative total morphine usage was 64.8 mg (SD 19.6) and 68.5 mg (SD 16.0), hardly suggestive of a linear relationship in the range 0.7 to 1.0 mg. Even the 0.4 mg bolus group received 51.9 mg (SD 13.2), which is nearly double the 27.4 mg (i.e. 0.4 of 68.5 mg) which might be expected in a linear relationship. Furthermore, the demands (both successful and unsuccessful) were fewer in the 1.0 mg group than in the 0.7 mg group.

It seems to me that an equally valid and more convincing conclusion from these data might be that there is a threshold dose necessary for effective PCA, and that above this (presumably up to a second threshold of increased risk) demands are, to a reasonable extent at least, a function of the amount of opioid received. None of this is to deny the concept that analgesic consumption in PCA is determined by many factors, nor the concept that it is important to choose an appropriate bolus size. More studies of the type undertaken by these authors are needed to ellucidate the matter further.

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Reference

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A reply

Dr Merry offers an alternative explanation of our observations (*Anaesthesia* 1990; **45**: 619–22) on the use of different demand dose sizes when morphine patient-controlled analgesia (PCA) is supplemented by an infusion. We agree with Dr Merry that there is likely to be a threshold dose size below which PCA becomes less effective. However, we do not agree that our results support the hypothesis that above this threshold (up to a second threshold) the rate at which patients make demands is a function of dose size. Dr Merry's interpretation is based on only the 0.7 and 1.0 mg doses, which appeared to be associated with similar amounts of demanded morphine. We found no basis for considering these two dose sizes separately from the 0.4 mg dose. As Dr Merry notes, we reported a significant linear trend component to increasing demanded morphine as dose size increased, but no significant deviation from linearity. Thus, we were unable to reject the hypothesis that, over the dose range studied, increased dose size results in more morphine being received. Although we speculated that the 0.4 mg bolus size may be suboptimal, patients receiving this reported similar levels of pain and satisfaction with pain relief to those receiving 0.7 mg or 1.0 mg boluses.

It may be that there is a range of dose sizes over which the rate of demands is inversely proportional to bolus dose size, but studies examining larger dose sizes may be necessary to determine this.

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Epidural diamorphine for the obstetric patient

Dr Stevens and his colleagues have demonstrated that epidural diamorphine can provide effective analgesia after Caesarean section (*Anaesthesia* 1991; **46**: 256–9). We were surprised, however, to read their interpretation of our previous study designed to investigate the analgesic effects of epidural diamorphine in labour.[1] They state in their introduction that 'a 5 mg dose of diamorphine epidurally has resulted in an unacceptable incidence of side effects in combination with bupivacaine in labour'. It is not clear to which side effects they are referring. In the study they have referenced, the only side effect which had a significantly higher incidence in the diamorphine group was pruritus. It is stated clearly in the paper that 14 of the 18 mothers who reported pruritus only did so after direct questioning, that is, they did not report it spontaneously. In only one mother was it sufficiently troublesome to merit treatment with naloxone. Dr Stevens and his colleagues did not ask their patients directly about pruritus, as they acknowledge in their discussion, and although no patients spontaneously reported this side effect, the incidence cannot be assumed to be zero.

In our paper,[1] only nine of 23 women who received diamorphine reported feeling drowsy, again on direct questioning. Dr Stevens *et al.* used a rank sedation score to assess sedation, and found that most of their patients experienced a degree of drowsiness 4 and 8 hours after administration of epidural diamorphine. Although these data are not comparable, there is nothing to suggest that the incidence of drowsiness was higher in the earlier study.

We suggest that a 5 mg dose of epidural diamorphine, administered with bupivacaine, does provide effective analgesia in labour, and its use is not associated with an 'unacceptable incidence of side effects'.

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Reference

1. MCGRADY EM, BROWNHILL DK, DAVIS AG. Epidural diamorphine and bupivacaine in labour. *Anaesthesia* 1989; **44**: 400–3.

A reply

Thank you for the opportunity to reply.

It is very difficult to compare the incidence of side effects between studies when different protocols have been used.

However, we do consider any side effect which requires specific additional treatment or which 'interfered with feeding of the baby' as unacceptable. As Dr McGrady and her colleagues suggested in their discussion, 'Perhaps a smaller dose, e.g. diamorphine 3 mg might limit some of the side effects'. Surely this implies an unacceptability of the side effects by these workers?

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Two incidents of complete failure of OAV 7750 ventilators

The Ohmeda OAV 7750 ventilator is designed to be used in conjunction with an Ohmeda Excel Anaesthesia System only, and consists of a control and a drive unit as a matched pair. Rebreathing or non-rebreathing patient system cassettes can be used, the bellows of which are then linked to the pneumatically operated, electronically controlled drive unit.

In both instances an Excel 410 anaesthetic machine was in use with a rebreathing cassette and a circle system. Routine machine[1] and circuit checks had been completed satisfactorily. After connection of the anaesthetic circuit the ventilator delivered three breaths to the first patient before the chest ceased to move, despite the ventilator cycling normally. Manual ventilation similarly failed to generate any positive pressure within the circuit. After connection of the second patient, the ventilator was again observed to cycle normally but failed to move the chest. However, this patient's lungs could be ventilated by hand. The patient system manometer was noted to read zero and did not move with either attempted mechanical or manual ventilation.

The rebreathing cassette features a pneumatic circuit let into the patient connection of the cassette for monitoring patient system pressure. Part of this circuit, underneath the cassette and hidden from view, consists of a moisture filter and a 11 cm length of neoprene hose (5 mm ID, 9 mm OD, Fig. 1). In the first incident this short hose had become disconnected, opening the ventilator circuit to atmosphere and rendering it impossible to ventilate the lungs mechanically or manually. In the second, the hose was found to be severely kinked, occluding it completely. Whilst this would render the pressure manometer inoperative, we have studied the cassette circuit diagram[2] and cannot explain why patient circuit pressure is lost.

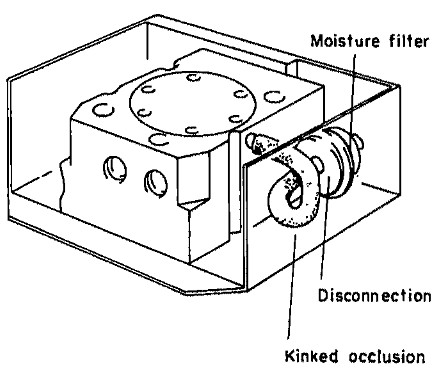

Fig 1. The OAV 7750 anaesthetic ventilator rebreathing cassette.

We believe the cause of both of these incidents to be a design fault in opposing the hose connections at 90°. This is compounded by the necessary requirement to detach the filter before weekly cassette autoclaving, degrading the friction fit of the neoprene rubber.

We have tried a local modification of replacing the neoprene tube with a section of 4.5 ID Portex armoured tracheal tube, with the reinforcing wire trimmed back by 5 mm at each end to allow tight push-fit over the connectors.

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S.J. Hunter
D.C. Laidlow

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A reply

We appreciate the opportunity to reply to the letter from Drs Spittal, Hunter and Laidlow, concerning our OAV 7750 ventilators. However, at the present time we do not have sufficient detailed information on this particular matter to permit us to make a full response to the letter, but we are working closely with the authors to investigate fully the issue described by them.

The Ohmeda range of OAV ventilators are designed with safety in mind and have in-built safety features, such as integrated alarms, which, although not mentioned by the authors, should have activated in the circumstances reported, thus making the clinician aware of an irregularity within the system.

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Ohmeda 9000 syringe pump

Like Dr Stokes and his colleagues (*Anaesthesia* 1990; **45:** 1062–6) I have been impressed with the Ohmeda 9000 syringe pump, having used it during research into infusion anaesthesia. The Ohmeda 9000 is unique amongst syringe pumps designed for anaesthesia (this group includes the Bard Infus O.R.* and the AMD PS6050†) in that a bolus rate of 1200 ml/hour can be administered. Whilst useful during infusion anaesthesia, it is potentially dangerous if used for epidural infusions or infusion of inotropes. The authors evaluated the pump in the intensive care unit and I presume they do not advocate its use in this setting. The manufacturers do not market the pump for use in the intensive care unit or maternity ward, although I would welcome it in these settings providing the bolus facility was modified or disabled.

At present there are only draft standards relating to the performance of infusion control instruments.[1] It would have been more informative if the authors had bench tested

the pump according to the draft format which has been published and used for many years at the Bath Institute of Medical Engineering.[1,2] I am interested to know if the output of the pump is continuous; the maximum excursion about the set rate; the start up time and the bolus on release of occlusion; the time to alarm following occlusion and both the short and long-term accuracy during infusion. Were the 10 ml syringes refilled during testing? Hopefully this information will be available in a forthcoming 'Evaluation' which replaces 'Health Equipment Information' as the reporting medium for electromechanical equipment.

The authors referred to the problem of stiction in 10 ml syringes. Anaesthetists may be tempted to refill 50/60 ml syringes[3] in the interest of economy, convenience or asepsis, but disposable syringes are provided with sufficient lubrication for single use only. With use there is a breakdown in the silicone lubricant. Refilling increases the stiction (i.e. the fractional force to be overcome to set one object in motion when it is in contact with another) between the plunger and barrel (Auty B., written communication). This does not always occur because the breakdown of lubricant is erratic and was not a frequent clinical problem with the older generation of syringe pumps.

The new generation of infusion pumps have a much lower occlusion alarm pressure than older models, usually around 50 mmHg as compared to over 1000 mmHg.[4] As stiction increases, the infusion pumps alarm for no apparent cause. This may result in the pump being returned for repair. Spurious alarms may lead to abandonment and disillusion with infusion anaesthesia or at worst patient awareness.

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Footnote

*Bard Ltd., Forest House, Brighton Rd., Crawley, West Sussex RH11 9BP.

†Advanced Medical Devices Ltd., Mantra House, Keighley, West Yorkshire BD2 1SX.

Does an acute pain service require a high dependency unit?

We refer to the recent report published by the Association of Anaesthetists entitled The High Dependency Unit (HDU).[1]

We were surprised by one of the conclusions drawn from the intensive care survey, namely that it 'was recognised that modern methods of drug administration, as for example in the relief of acute pain, require closer supervision than may be available on the general wards'; the joint College report was referenced as supporting this view. The implication is that Dr Wildsmith's working party believe the level of care available on general surgical wards is inadequate for the management of patient controlled analgesia (PCA) or extradural opioid infusions. Our opinion is that the recent joint College report[2] contradicts this view. In this report our College clearly states that, though an HDU/ITU facility is desirable for the management of high risk patients, 'any ward designated for the care of patients recovering from major surgery should have enough trained nurses and doctors to care for patients requiring intramuscular analgesia, PCA or epidural analgesia'.

The provision of an HDU as an intermediate between recovery room, ITU or the general ward for the increasing numbers of high risk patients we now anaesthetise, irrespective of the mode of analgesia employed, is a concept we fully support. So too is the setting up of an acute pain service to bring to an end decades of 'morally and ethically unacceptable' postoperative pain.[2] The High Dependency Unit report links the setting up of an acute pain service with the provision of an HDU. Such a linkage will at least hamper and at worst prevent the setting up of acute pain services.

We must decide whether, as our College believes, surgical wards are adequately staffed to take on new analgesic techniques; or, as our Association believes, HDUs are required for the supervision of patients receiving analgesics administered by modern methods.

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J.R. WILES

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A reply

Thank you for the opportunity to comment on the letter from Drs Watt and Wiles. By quoting (and taking) one section from each report out of context they have attempted to demonstrate a dichotomy of opinion between the joint Colleges report on postoperative pain and the Association report on high dependency care. I do not believe that this dichotomy exists. There are differences in emphasis, but then the two groups were considering two topics that only overlap to a moderate degree.

First, I should make it quite plain that it was not the Association working party that '... *recognised that modern methods of drug administration ... require closer supervision than may be available on general wards'*, but the clinicians who took part in the intensive care survey. In confirmation of this I hear many people say that they do not feel that it is safe to use epidural opioids on the general wards of their hospitals.

The Colleges report does say that '... *any ward designated for the care of patients recovering from major surgery should have enough trained nurses and doctors to care for patients requiring ... epidural analgesia'*. However, I take the use of the word *'should'* to imply a recognition that this is desirable, but not necessarily always the case. Further, the statement is followed by a list of no less than

five provisions and then the following *'If resources are made available . . . epidural opioid analgesia should not need to be restricted to HDUs'*. If indeed the resources listed are available I would agree that a patient receiving epidural opioids may be nursed safely on a general ward, but then that general ward will not be so very far away from fitting within our definition of a high dependency unit anyway!

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Pain and basic human rights

There were editorial responses in many journals to the report of the Royal College of Surgeons and the College of Anaesthetists on pain after surgery.[1] Dr Harmer in his editorial in this journal (*Anaesthesia* 1991; **46:** 167–8) picked out many areas of inadequacy and made sensible suggestions leading to his general conclusion that better care needs more money.

Where Dr Harmer weakened his arguments was in his use of rhetoric. Anyone with knowledge of sadomasochistic videos knows that they are not in any way similar to postoperative wards. Sadomasochism is a perversion in which pain is enjoyed by giver and receiver; patients may suffer pain by neglect but not by intention, and no nurse or doctor wishes their patients to be in pain. The editorial then concludes with a quote, which has been used also by Abbott Laboratories Ltd in their advertising for a device for patient-controlled analgesia: 'by any reasonable code, freedom from pain should be a basic human right'.[2]

A basic human right must be universal, absolute, and indivisible. When a patient in an affluent democracy fails to get adequate pain relief from an injection of papaveretum, it may be unsatisfactory medical care, it may reflect, to quote Dr Harmer, 'a lack of will and finance', but it is not denial of a basic human right. It cannot even be a Utopian ideal; the only people who truly have freedom from pain are those who suffer terribly by its congenital absence. The idea of basic human rights must not be devalued by allowing the phrase to become a cliché, used by pressure groups to attract attention.

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A reply

I thank you for your interest in my editorial and I accept some of the points. My misuse of the term sadomasochistic rituals must, I fear, relate to my nonfamiliarity with such video productions and I am thus guilty of speaking from a position of personal inexperience. I hope though that you will except a degree of editorial license. As for the conclusion, I believe we are guilty of not providing adequate analgesia to our patients and in an affluent democracy perhaps this is a denial of basic human rights. I regret that Abbott Laboratories have chosen to use the same quotation, but as it appears in the Joint College Report I feel that we are not insular in our belief.

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M. Harmer

Regional anaesthesia and cough effectiveness

The work of Harrop-Griffiths *et al.* (*Anaesthesia* 1991; **46:** 11–3) reporting the effects of spinal and epidural anaesthesia on respiratory function tests produced results similar to my own on mothers having Caesarean section under epidural anaesthesia. In addition to the respiratory measurements made by Harrop-Griffiths *et al.*, preblock and pre-incision, I reported further consequent falls in peak flow during Caesarean section under epidural anaesthesia at a time when the abdomen was open.[1]

Studies on a further 17 patients having Caesarean section under spinal anaesthesia have yielded a similar pattern of peak flow measurements. From mean baseline preoperative readings of 404.7 litres/minute (SD 55.1), the peak flow fell to mean levels of 370 litres/minute (SD 54.5) when the block was fully established and before the abdomen was opened. Peak flows were measured again after the delivery of the baby but before peritoneal closure, and had fallen further to mean levels of 314 litres/minute (SD 58.9). This reduction in peak flow from the baseline reading was statistically significant ($p < 0.01$). The mean weight of the mothers was 72.2 kg (SD 5.4) and their mean height was 156.3 cm (SD 7). The mean block height was to T_4 and the mean Bromage score of motor block was 3. As in the epidural group, the lowest measurements were the intra-operative readings. However the mean lowest reading of 314 litres/minute (SD 58.9) in the spinal group reported here, was still well above the figure of 200 litres/minute which may be associated with the inability to initiate an effective cough.

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Reference

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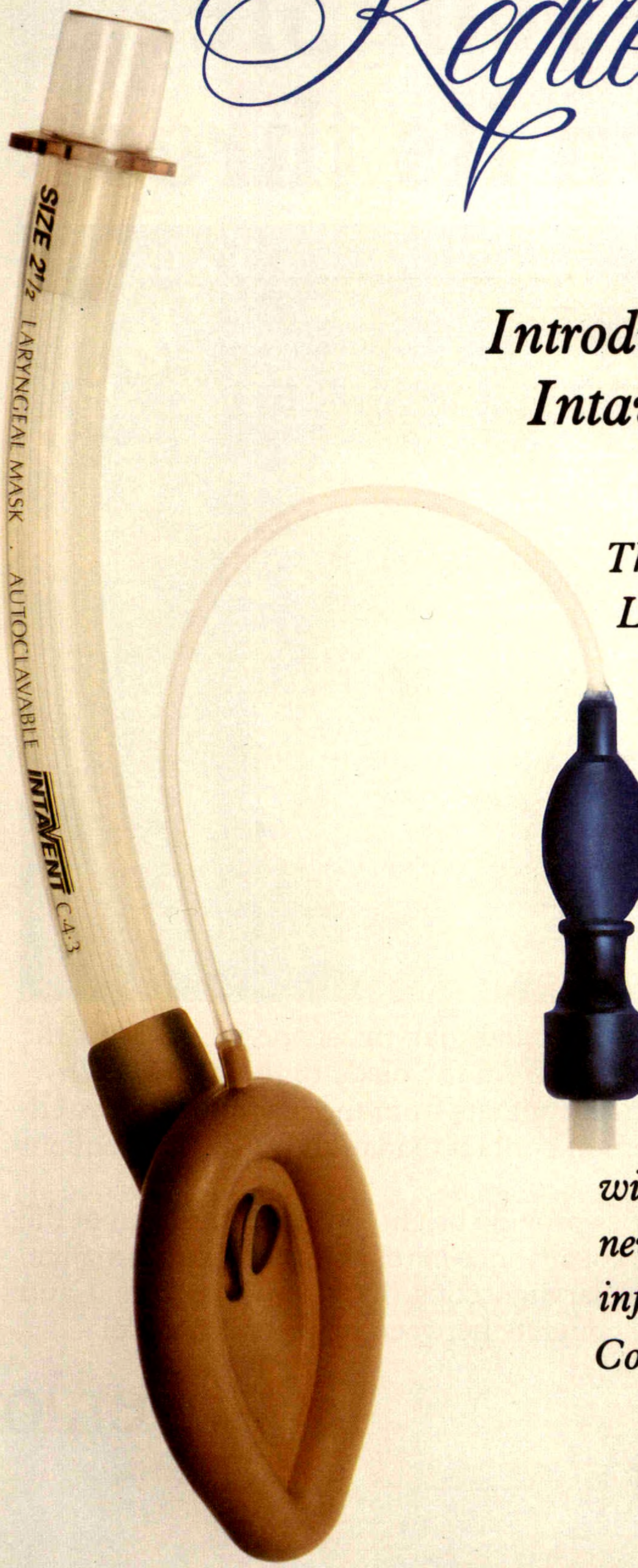
…as Requested



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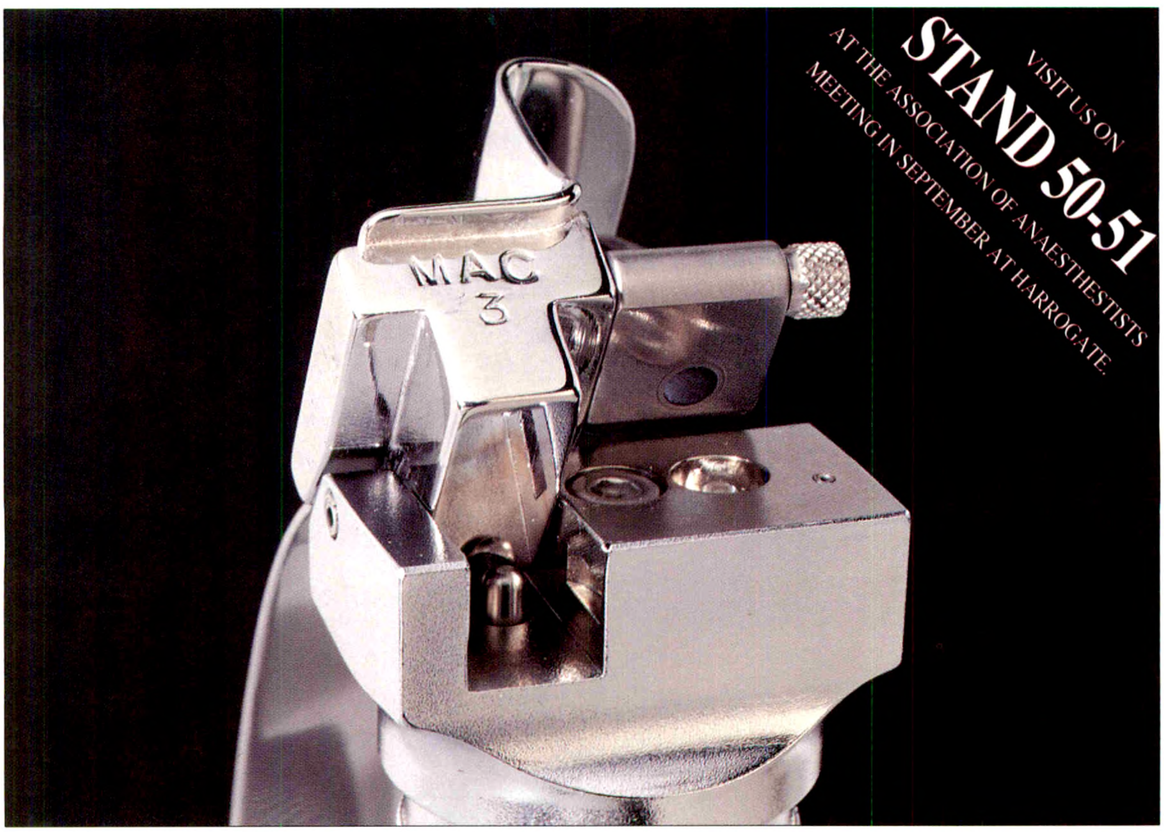

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Polarisation of a 2.5 mm tracheal tube

Within the last 18 months, six extremely premature infants have presented for cryotherapy to areas of retinal detachment due to retinopathy of prematurity. Their gestational age at birth ranged from 24 to 27 weeks; mean birth weight was 770g (600–1200.) When the first infant presented for surgery, he was big enough to accept a 3.0 mm south polar tracheal tube (Portex Limited.) The other infants, however, presented at a younger age and a 2.5 mm tube was more appropriate.

In such small subjects, there is inevitably competition between surgeon and anaesthetist for the space around the infant's face. A polar type of tracheal tube is useful to bring ventilator connections and gas sampling devices away from the surgical area. In the absence (to our knowledge) of a commercially available south polar 2.5 mm tracheal tube, the solution to the problem was found in a standard textbook of anaesthesia.[1] A small tracheal intubation stylet (Portex Limited) was stripped of its plastic coat and introduced into an uncut 2.5 mm tracheal tube. This was moulded to the desired shape as illustrated in Figure 1 and autoclaved. When cooled, these tubes have provided a very satisfactory airway for these procedures which last up to 3 hours. The demand for 2.5 mm polar tracheal tubes is likely to remain too small to justify commercial production. We have found these home-modified tubes to be reliable and easy to use in these occasional circumstances.

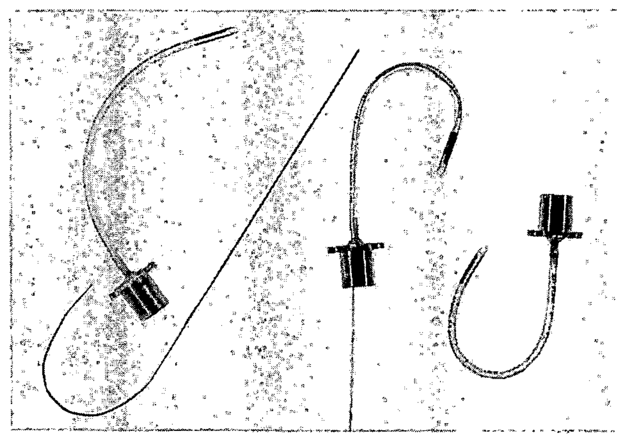

Fig. 1

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Reference

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The length of RAE preformed tubes

We read with interest the report by Black and Mackersie (*Anaesthesia* 1991; **46:** 42–3) on accidental bronchial intubation with RAE tubes. Their reported high incidence of tube misplacement has prompted them to conclude that bronchial intubation is indeed possible while using RAE tubes. We have recently had an experience which may provide additional insight into this conclusion. A 5-year-old boy was scheduled for a tonsillectomy and a size 5.0 mm ID RAE tube was selected. However, before intubation it was realized that the tube seemed to be unduly long. When compared to a second tube, from the same lot, the difference became obvious (Fig. 1). Both tubes were identically packaged as Mallinckrodt Critical Care (MCC), although the longer tube was stamped as a Mallinckrodt Laboratories Ltd. (MLL). How many of the longer version were packed as 'MCC tubes' is not known. In relating our experience to the results of Black and Mackersie, it is unfortunate that the nature of the RAE tubes used in their retrospective analysis was not specified. During the latter part of 1986 and the beginning of 1987, the length of the RAE paediatric tubes was reduced by 0.5 to 1.5 cm depending on the ID for the European market. The difference in length between the size 5.0 MLL and the size 5.0 MCC RAE Mallinckrodt tube is 1.5 cm. Given these considerations, may we suggest that final judgement on RAE tubes cannot be made without the specification of the tubes used in the study. It remains speculative whether our finding was a singular event or whether the same packaging situation might have led to the unintentional use of relatively long tubes in their study population.

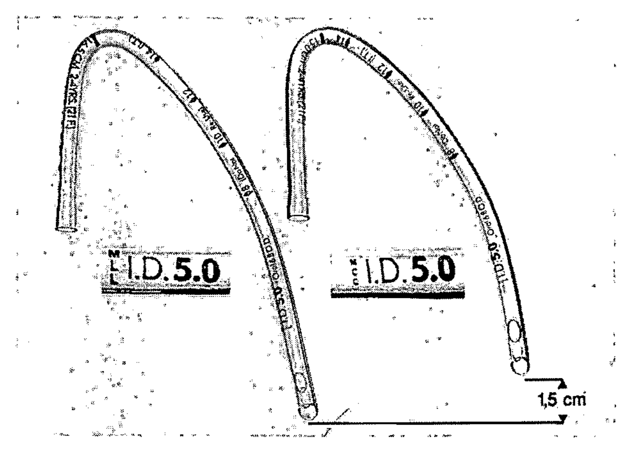

Fig. 1. Two Mallinckrodt preformed tubes of identical diameter size, but different lengths. Insets are magnifications of tube markings.

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Drs Black and Mackersie (*Anaesthesia* 1991; **46:** 42) provide eloquent testimony to the recognised complications which can arise because RAE (Ring-Adair-Elwyn) preformed tracheal tubes are occasionally too long when used in the age-related sizes recommended for children by the manufacturer, Mallinckrodt. Nevertheless their paper invites some critical comment. Although it is clear from the main text of their article that they conducted a retrospective study of hospital case notes, Drs Black and Mackersie state in their summary (which will no doubt be used by abstracting services) that they studied a group of 40 patients. This distinction is not pedantic: they have no way of knowing when the RAE tubes used in these patients were manufactured, an important consideration because the Mallinckrodt Company shortened the lengths of paediatric RAE tubes below and including the 5.5 mm size in 1986. Consequently, it would be helpful to know the calendar years spanned by the cases in their study. Even if

their cases postdated 1986, it would be no guarantee that the RAE tubes used were of the new shorter variety. Much would depend upon the rotation of stock at their hospital. I have lately found RAE tubes in the tiny sizes stamped with a 1984 date of manufacture in the anaesthetic room drawers of three out of six of the main operating theatres in this hospital. These tubes were presumably not discarded because the stamping of packaging wrappers with a 5 year expiry date is a relatively recent requirement for manufacturers.

Would Drs Black and Mackersie agree in the light of my remarks that their reported high incidence of complications with RAE tracheal tubes might not be quite as applicable to current clinical practice as they claim in their paper?

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A reply

Thank you for giving me the opportunity to reply to the above letters.

Dr Black and I were well aware that the RAE tubes had been shortened in 1986. The study was conducted on patients having myelography in less than 6 months between late 1987 and early 1988. We have a policy whereby only 6 weeks supply of RAE tubes are held at source, with an expected annual use of over 1800 tubes under size 6.0, with equal use of all sizes between 3.5 and 6.0. It is therefore almost certain that the tubes were of the shorter pattern.

The real learning point is that a preformed tube of correct diameter is *not* necessarily the correct length for all children. Anaesthetists should be alert to the possibility of bronchial intubation or the smaller risk of the tube being too short. The Murphy eye only makes the diagnosis of bronchial intubation more difficult, and while both lungs may ventilate on auscultation after intubation, movement of the patient (as in the case which triggered our study) or use of a mouth gap, may lead to inadequate ventilation and arterial desaturation.

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Another antipollution device for the Jackson–Rees modification of Ayer's T-piece system

Most suggestions for disposal of gas from the Jackson–Rees modification of Ayer's T-piece affect the convenience of the system. Many different types of scavenging devices have been described[1-5] and I wish to report another system which utilises a Portex Minilink T-piece without affecting the simplicity of Ayer's T-piece.

The system (Fig. 1) requires the connectors available from recently marketed Portex Minilink equipment for anaesthesia (Portex Ltd England). One 8.5 mm Ayer's T-piece with 15 mm connector (Part No 100/266/015) is used in the normal way for the delivery of fresh gas and the second is used for scavenging. The distal end of the expiratory limb of the T-piece is fitted with a suitable connector which can accept the 8.5 mm end of the T-piece on the internal diameter and the bag mount of the external diameter (Part No 1355263 tracheal connector, BOC Health Care). When scavenging of gases is desired, the 8.5 mm end of the scavenging T-piece is connected to the distal end of the expiratory limb and the 15 mm connector to a 750 ml open ended reservoir bag fitted with a bag mount (Part No 100/277/000) which is then occluded. The fresh gas port of the scavenging T-piece, which will now work as the outlet for the gases, is threaded over the narrow end of a blue 7.5 mm tracheal tube connector. Alternatively, a simple tubing of appropriate diameter can be incorporated between the outlet and the tracheal tube connector. This is in turn fitted to a standard 30 mm ISO male taper hose connector. The female taper hose connector, with a suitable length of transfer tubing (white scavenging tube), is connected to the exhaust pendant (scavenging system with reservoir and relief valve) on the anaesthetic machine.

The total resistance of the system, over the flow range of 3–20 litres/minute is not significantly increased by the addition of the scavenging T-piece. However, there are some potential problems which should be borne in mind. The scavenging system should be dismantled if there is a need for assisted ventilation and a separate 750 ml open-ended bag should be ready at hand. Constant vigilence for disconnections is required. Accidental exposure of positive or negative pressures has not been a problem because the system was connected to the scavenging pendent with the relief valve on the anaesthetic machine. However, a simple

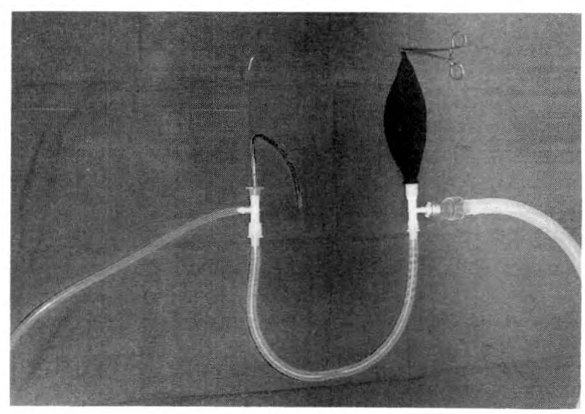

Fig. 1.

pressure relief valve can be incorporated in the system should the anaesthetist worry about the build-up of pressure in the circuit. This system should not be used with active scavenging devices and addition of a large air inlet at any point after scavening connector will be desirable. In over 2 years at this hospital, no problems have emerged from its use. This system is only suitable for spontaneously breathing patients and is easy to assemble.

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Lumbar plexus block after total knee replacement

It was interesting to read the report by Serpell and colleagues on lumbar plexus block after total knee replacement (*Anaesthesia* 1991; **46:** 275–7) and I would like to comment on their conclusion. As in our preliminary study (with the block performed *before* surgery),[1] Serpell demonstrated that patients with the lumbar plexus block required a third less morphine than the control group, but postoperative pain scores and the incidence of side effects were comparable. However, it is debatable whether a 35% reduction of total 48 hour consumption of morphine justifies the use of an invasive procedure (although safe and simple), when no other advantages such as a reduction in pain or side effects seem to be accomplished. The use of noninvasive procedures such as fixed NSAID regimens have been demonstrated to be even more effective, with a reduction in opioid requirements of up to 50% following major orthopaedic surgery,[2] and in some studies with fewer side effects as well.[3] It is my opinion that the introduction of an invasive method for postoperative pain relief is justified only by a substantial reduction in pain, opioid requirement or morbidity, and this does not seem to be accomplished with lumbar plexus block in knee arthroplasty.

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The study of Serpell *et al.* (*Anaesthesia* 1991; **46:** 275–7) showed that 0.5% bupivacaine with adrenaline 1 in 200 000 (0.3 mg/kg) in the femoral neurovascular sheath resulted in less morphine requirement than a control group and that pain scores in the two groups were similar after total knee joint replacement. Modification of their local anaesthetic technique is likely to achieve reliable postoperative pain control much superior to conventional opioid analgesia.

Appropriate nerve conduction block pre-operatively, in addition to subarachnoid block (SAB), may influence the nature of de-afferentation of the operation site. In one of their references the authors cite that abolishing sensory input before the occurrence of painful stimuli reduces postoperative analgesia requirements and in their discussion they say a 3 in 1 femoral nerve block (FNB) was performed 'before spinal anaesthesia wore off'. This is an oversimplification; the time course of recovery and central processing of propagated action potentials of various modalities in the spinal cord after SAB are not well understood. Partial recovery might enable some such processing of sensory input in the brain before the return of conscious sensation (normality) in the relevant dermatomes, with resultant priming for subsequent pain perception.[1]

FNB, using a femoral sheath cannula and a single shot sciatic nerve block, can be inserted immediately after SAB in the anaesthetic room. This allows accurate visualisation of evoked responses. Movement of the patella by quadriceps contraction using a nerve stimulator ensures accurate nerve localisation and complete FNB after injection. Contraction only of the medial muscles of the thigh with minimal patellar movement results in a partial block and subsequent inadequate pain control. Other disadvantages of FNB insertion after the completion of surgery are that the surgical wound distorts or completely veils the normal patellar evoked response and the procedure must of course precede the application of a wound dressing.

The quality of conduction nerve block depends on the accuracy of needle or cannula placement before deposition of local anaesthetic and to achieve success the best conditions for producing an evoked response should be sought. Pre-operative nerve conduction blockade in addition to SAB therefore seems logical and total pain control can reliably be achieved after knee replacement using one or at most two 'top ups' through the femoral cannula, as described, 8 hourly. The need for opioid supplementation should be obviated, although non-steroidal anti-inflammatory drugs are a useful addition particularly in patients who have systemic joint disease. Nausea can still occur in the absence of opioids where there is total pain control produced by nerve blockade; at worst this is an improvement on nausea combined with pain.

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A reply

Thank you for the opportunity to comment on the points made by Drs Levack and Dahl.

Dr Levack is correct that accurate placement of local anaesthetic within the nerve sheath is crucial for success. The femoral nerve supplies branches to the rectus femoris and medial, intermediate and lateral vastus muscles of the thigh.[1] If the stimulating needle is inserted as proximally as possible (just below the inguinal ligament) and before these branches leave the sheath, then success of the block should not depend on which muscle is seen to contract. Provided the current required is less than 0.5 mamp, the risk of directly stimulating the muscles is also avoided. His suggestion of performing the block before surgery, however, would make assessment of the muscle response easier.

The process of central sensitization which produces allodynia, wind up and an increase in receptor field size is not fully understood.[2] It occurs primarily in the dorsal root ganglion, in which case a subarachnoid block (SAB) would have been thought sufficient to block it temporarily. Surprisingly, even with a clinically effective SAB, somato-

sensory evoked potentials are often able to pass to the cerebral cortex.[3] Therefore we agree that establishing a nerve conduction block in addition to SAB prior to surgery may be more effective at preventing the 'priming for subsequent pain perception'. However, there is no doubt that when a successful block is instituted, even postoperatively, on a patient in pain, the results are dramatic.

We must apologise to Dr Dahl and his group since, unlike their major study, the block in their second study was in fact given before surgery.[4]

A reduction in total 48 hour morphine consumption of only 35% is disappointing, but the results are so successful in some patients that we feel that more attention to the technical aspects, to ensure a higher success rate, more than justifies the invasive nature of the procedure. The knee mobiliser may have displaced some catheters by flexion of the hip and failure to top-up in time causes dramatic return of pain. The results could be further improved by more frequent administration or continuous infusion of local anaesthetic. Plasma levels from a previous study suggest that we could have given twice the amount of bupivacaine and still have remained within subtoxic levels.[5] To achieve complete analgesia would require additional blockade of the sciatic nerve.

NSAID regimens should certainly improve pain relief but we doubt the results would be as impressive as in total hip replacement which, from clinical experience, seems to be more easily controlled.

We hoped by the study to draw attention to the potential for alternative methods of postoperative analgesia in total knee surgery and encourage more doctors to evaluate what we feel is an excellent and safe method.

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'Spinal' headache — with no headache

A fit 24-year-old woman received a spinal anaesthetic for elective Caesarean section. A 26 gauge spinal needle was easily inserted at the $L_{2,3}$ interspace and the procedure passed uneventfully. Twenty-four hours later she complained of neckache, exacerbated by standing, but denied any headache or other symptoms associated with dural puncture. Systemic analgesics were administered, with little benefit. The neckache persisted, and was worse on standing up and on any neck movement, particularly rotational, when lying down. She consistently denied any headache, photophobia, nausea or vomiting. Pain limited mobilisation and childcare was difficult. Examination revealed an acutely tender area at the back of the neck, over approximately C_{2-4} vertebrae, extending over the occipital processes. There was no obvious swelling, but prolonged palpation was impossible due to acute tenderness. All movements of the neck were severely limited by pain. Application of abdominal pressure failed to relieve the pain, although moderate obesity and wound pain limited the pressure applied. There was no evidence of pain or swelling over the insertion point of the spinal needle. The patient was warm and sweating, and the possibility of meningitis was raised. However, she was apyrexial with a normal white cell count, and the postural nature of the neckache encouraged us to associate it with dural puncture.

We therefore decided to proceed with a blood patch. The patient sat up for the procedure, as her wound felt more comfortable in this position. At this point, and for the first time, she reported feeling a slight headache 'at the back of her eyes'. As previous experience had suggested that small volumes of saline injected into the epidural space often temporarily alleviates pain related to dural puncture, 10 ml saline was injected into the epidural space. The patient reported immediately that her neckache was relieved, confirming our diagnosis. A blood patch was subsequently performed and 20 ml autologous blood injected through the same epidural needle. Examination revealed that her neck was now completely pain free, and she had a full range of movement. Neckache did not recur, and she was discharged home some days later.

Headache after dural puncture is usually treated as a 'spinal' headache until proved otherwise. We are unaware of previous reports of this distressing complication presenting with neck pain alone, although neckache has been described as a component of the syndrome, in association with headache. In this case, the unusual presentation delayed effective treatment by a few days. Perhaps this report emphasises the importance of the postural feature of pain, and we hope this will assist others in their differential diagnosis of neckache after dural puncture.

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Ventricular fibrillation during examination of nose

A fit, 9-year-old girl weighing 28 kg, who had been investigated for dysmorphic facies and who was found to be chromosomally normal, presented for examination of her left nostril under anaesthesia. Following premedication with oral atropine 0.85 mg anaesthesia was induced with thiopentone 150 mg. Suxamethonium 30 mg was administered and the trachea intubated with a 6.5 mm uncuffed tube. Ventilation with 1% halothane in 66% N_2O

in oxygen was started by hand via a Bain circuit. Five minutes into the operation, without informing the anaesthetists of their intention to do so, 0.5 ml cocaine paste (25% with adrenaline 0.18%) was applied to the left nostril and the nose was immediately instrumented. The ECG showed multifocal ventricular ectopic beats which deteriorated into coarse ventricular fibrillation within 10 seconds. The halothane was switched off and the patient's lungs ventilated with 100% O_2. Two precordial 'thumps' were administered which had no effect on cardiac rhythm. External cardiac massage was started. Within 2 minutes the child had reverted spontaneously to sinus rhythm without defibrillation or drugs. However, lignocaine 1 mg/kg was administered to prevent recurrence of the arrhythmia. The operation was abandoned when on initial inspection the nose seemed clear. The child was woken up and made an uneventful recovery. A12 lead ECG in recovery revealed a sinus tachycardia, but no other abnormality. ECG was monitored overnight with no further arrhythmias. The patient was re-investigated by the paediatric team and it was confirmed that there was no detectable cardiovascular anomaly.

There are a number of reasons why this child could have developed an arrhythmia. Although an association between hypertelorism and cardiac anomalies has been described in the literature,[1] this usually occurs as part of a larger symptom complex, the other elements of which were not exhibited by this child. Furthermore, there was no clinical evidence of underlying cardiac anomaly. A nasocardiac reflex has been described.[2,3] Physical, chemical and thermal stimuli to the nose may cause widespread cardiovascular and respiratory responses.[2] This reflex is thought to occur via sensory nerves and the neuropeptide substance P is the suggested transmitter. Cocaine is used during surgery on the nose principally for its vasoconstrictor action.[4] The drug inhibits reuptake of noradrenaline at sympathetic nerve terminals and this accounts for its effects on the cardiovacular system.[5] Uptake of cocaine into the circulation is slowed by addition of adrenaline,[4] however, this further increases circulating catecholamines and increases the potential for tachyarrhythmias, especially in the presence of halothane anaesthesia.[6] In one study, intranasally applied cocaine 1.5 mg/kg was absorbed rapidly but no important cardiovascular effects occurred in the presence of halothane anaesthesia.[7]

It seems likely therefore that ventricular fibrillation in this case was caused by sympathomimetic substances in the presence of halothane anaesthesia during a stimulating procedure.

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Duplicate markings on an epidural catheter

A 26-year-old primigravid patient requested an epidural for pain relief in labour. An intravenous infusion was set up, the patient placed in the left lateral position and the lumbar spine area sterilised with iodine and alcohol. A 16 gauge Tuohy needle, epidural catheter (B. Braun) and filter were provided. The L_{2-3} interspace was chosen and the epidural space was identified at a distance of 4 cm from the skin by a loss of resistance to air technique. The epidural catheter was threaded smoothly into the epidural space and the needle removed. The catheter was then slowly withdrawn so that the desired length would remain in the epidural space. However, it was noticed that there were two identical markings, both with three bands, 5 cm apart. To avoid confusion and any possible complications, the catheter was removed and examined. When comparison was made with another epidural catheter with correct markings, the catheter in question had a mark with three bands instead of the standard two bands at a distance of 10 cm from the tip. At the point of 15 cm from the catheter tip the correct standard three band marking could be found (Fig. 1).

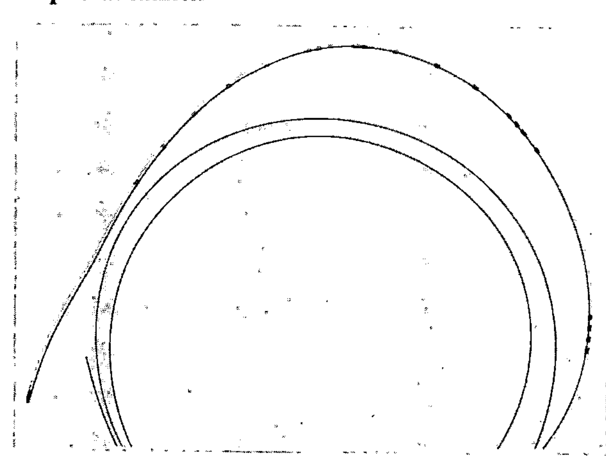

Fig. 1.

Marks on epidural catheters indicating distance from the tip of the catheter were introduced to allow accurate estimation of catheter length in the epidural space.[1,2] Most catheters have a two band mark to indicate 10 cm and a three band mark to indicate 15 cm from the catheter tip. The incorrect marking may lead to errors in estimation of catheter length remaining in the epidural space and the catheter may end up being withdrawn further than intended. This case again illustrates the importance of checking all equipment before attempting any form of regional block.

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A reply

Perifix epidural catheters are printed in a concealed and automatic machine, in a continuous and set procedure. The manufacturing system does not, under normal circumstances, allow for such a mistake to happen. A theoretical explanation for a duplicate printing is a short-term power supply cut in the printing machine. Over the years B. Braun has manufactured millions of epidural catheters and no such incident has been reported previously. We consider this finding as an isolated incident. It is with regret that the catheter passed through the quality control system and we apologise for any inconveniences caused.

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A. Berent
H.J. Otto

Raised intra-abdominal pressure and renal failure

I read with interest the letter by Drs O'Leary and Park (*Anaesthesia* 1991; **46:** 326–7) on the subject of acute renal failure associated with use of the pneumatic antishock garment and agree that raised intra-abdominal pressure should always be considered as a cause of oliguria in susceptible patients. These include those who have had abdominal aneurysm repair and those who have suffered abdominal or pelvic trauma, as a case experienced illustrates.

An 11-year-old girl presented with severe pelvic trauma following a car crash. This resulted in disruption of internal iliac vessels; she required massive blood transfusion (60 units) and interventional radiology to control haemorrhage. Hoffman external fixateurs were used for stabilisation of the pelvic fractures. Subsequently she remained cardiovascularly stable, but was noted to have a markedly distended abdomen and oliguria. A decompressive laparotomy was undertaken; large amounts of organising retroperitoneal clot and severe oedema of the tissues were noted. Due to the friable nature of the tissues it was not possible to evacuate all the clot. Rather than close the abdomen conventionally, a Marlex sheath was inserted to cover the abdominal contents and the abdominal musculature left open. On return to the Critical Care Unit she exhibited a brisk diuresis. The abdominal defect was repaired at a later date.

As well as being aware of the dangers of raised intra-abdominal pressure on renal function, we should consider the routine monitoring of abdominal pressures. This can be done directly through an intra-abdominal catheter or indirectly via an indwelling bladder catheter as described by Mansberger and Watlington.[1] This is simple, cheap and safe and would provide useful information on which patients would benefit from decompressive laparotomy.

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Reference

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Accidental intra-ocular vecuronium

We would like to describe an incident which happened earlier this year. A senior operating department technician (ODT) was mixing up some vecuronium in the anaesthetic room, to the usual concentration of 10 mg in 5 ml of water. (It is standard policy in our hospital to allow trained staff to do this. The ampoules are retained for inspection by the anaesthetist.) On removing the needle from the rubber bung in the top of the ampoule about 1 ml (2 mg) sprayed out through the hole made by the needle, most of which went into his eyes. He immediately reported the incident to the consultant anaesthetist in the operating threatre and was instructed to wash his eyes out with a liberal quantity of water. Initially there seemed to be no problem, but after 3 minutes he complained of feeling flushed and weak. He then said he was having difficulty in breathing and swallowing and was laid down on a trolley. He was unable to sustain a headlift. On direct questioning he gave no personal or family history of any prior myasthenic or neuromuscular symptoms.

As his symptoms were rapidly worsening it was felt expedient at this stage to administer an anticholinesterase as a therapeutic test. Neostigmine 2.5 mg premixed with glycopyrronium 0.5 mg was given slowly intravenously. There was no symptomatic improvement, indeed the patient felt worse. He started to salivate and complained of abdominal colic. Coarse fasciculations were noticed in his forearm muscles. Atropine 0.5 mg was given intravenously with some relief of the abdominal pain. Over the next 30 minutes his other symptoms gradually improved. He was examined by a medical registrar who could find no gross neurological or muscular abnormality. He subsequently resumed his normal duties.

It is well known drugs can be absorbed rapidly from the eye to produce systemic effects and it is possible that significant absorption of vecuronium occurred in this case. However, there was no objective evidence to support this theory. Throughout the episode he denied diplopia. In addition there was no ptosis or other sign of muscle weakness. By contrast the effects of the neostigmine were clearly seen. It would seem that 0.5 mg glycopyrronium was insufficient to prevent the muscarinic effects of neostigmine on the bowel or salivary glands. The lack of subjective improvement and the occurrence of fasciculations after the administration of neostigmine would suggest there was no significant competitive neuromuscular blockade. In retrospect it would clearly have been useful to have performed peripheral nerve stimulation tests before giving the neostigmine.

Since this event we have re-emphasised the usual advice to those making up drugs. This includes injecting only a small abount of water into the ampoule to dissolve the drug, and diluting it to its final volume in the syringe. In addition, a similar quantity of air should be removed from the ampoule before injecting the water. We doubt this is the first time a muscle relaxant has accidentally entered the eyes, but a literature search back to 1981 has not revealed any reports of paralysis following such an event. Whilst it is possible that this was an hysterical reaction, we think it unlikely. The ODT concerned is a senior and experienced member of the department and was initially dismissive of the incident when he reported it to the consultant. The symptoms appeared only after a latent period compatible with the known onset time of vecuronium. We wonder if any readers have witnessed similar incidents and whether any systemic effects resulted.

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Amorous behaviour? Be discreet

We welcome the correspondance generated by our letter on amorous behaviour or sexual fantasy after general anaesthesia or sedation (*Anaesthesia* 1990; **45:** 699) but defend our custom of informing patients pre-operatively. A recent paper by Lonsdale and Hutchinson suggests that the patients desire for pre-operative information may have been previously underestimated.[1] We accept that warning patients indiscreetly, using terms such as 'sexual fantasy' and 'amorous behaviour' may provoke alarm. In practice, we tactfully assure our patients by telling them pre-operatively that 'pleasant vivid dreams can occur'. We believe that this simple communication, whilst neither being unbecoming nor provoking anxiety, is sufficient to reduce any patient distress precipitated by drug-induced amorous behaviour, sexual dreaming or fantasy.

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Reference

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Acute choreoathetoid reaction to propofol

We read with interest the report by McHugh[1] concerning a woman showing an acute choreo-athetoid reaction during induction of anaesthesia with propofol. Spontaneous movements have been reported both in adults and children, but with a higher incidence in the latter group.[2] We recently demonstrated that these movements were not related to any cortical epileptic activity but rather to the involvement of deep subcortical structures.[3] We also showed that increasing the induction dose of propofol from 3 mg/kg to 5 mg/kg decreased significantly the incidence of spontaneous movements in children.[3] No precise explanation concerning their origin is presently available. However, we believe that an imbalance between cortical and subcortical effects of propofol might be involved in the genesis of these movements. In view of this hypothesis and the known pharmacokinetics of propofol (very short $T_{\frac{1}{2}}\alpha$) we would not recommend inducing anaesthesia by repeated low doses of propofol (e.g. 40 mg every 10 seconds as reported in the present case) since this technique may only accentuate the the imbalance between cortical and subcortical deepness of anaesthesia, thus promoting the appearance of spontaneous movements.

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Propofol and excitatory sequelae in dogs

The case detailed by Dr McHugh (*Anaesthesia* 1991; **46:** 425), of an acute choreoathetoid reaction to propofol, is one of a series of similar reports in the medical literature (dating back to 1987)[1–3] and was of considerable interest to us, since we have encountered similar phenomena in dogs. Propofol is regularly used for the induction and maintenance of anaesthesia in dogs and cats. It is generally considered to be a safe and reliable agent, which produces rapid and pleasant recovery. Some of the initial trials in dogs led workers to observe that, while there appeared to be few problems associated with the drug when employed for induction alone[4,5] its use as a continuous infusion for maintenance of anaesthesia was linked with a number of unusual reactions. These included shivering, muscle tremors, paddling and extensor rigidity with opisthotonus and were reported in nearly one third of the animals anaesthetised.[6] More recently, similar sequelae have been seen in cases where propofol has only been used for induction. These observations, taken in conjunction with the increasing numbers of reports in the medical literature of excitatory phenomena associated with the use of propofol, led us to examine our recent records of canine anaesthesia with the aim of documenting the nature and incidence of such reactions.

In a 2-month period in 1990, 148 dogs were anaesthetised with propofol. They were premedicated with a variety of agents, depending on their temperament, fitness and the procedure to be performed. Induction of anaesthesia was by an intravenous injection of propofol (4 mg/kg to premedicated animals and 6 mg/kg to unpremedicated ones) given over about 20 seconds. In the majority of cases anaesthesia was maintained using halothane or isoflurane, with or without nitrous oxide, in oxygen. Five dogs, undergoing bronchoscopy, were given a propofol infusion and supplementary oxygen. Most of the anaesthetics were uneventful. However, signs of possible central nervous excitement were reported in 12 cases. Manifestations included panting (three cases), muscle twitching (three cases), violent paddling movements (six cases), opisthotonus (four cases) and periodic rigidity of one or more limbs (three cases). These were seen mainly at induction and early maintenance of anaesthesia, although two animals showed extensor rigidity of one or more legs on recovery. Where this activity interfered with the surgical procedure, diazepam was administered and abolished or reduced the reactions. There were no apparent cardiovascular or respiratory problems during these episodes and animals behaved normally on recovery from anaesthesia. Several dogs, in which untoward events occurred, were anaesthetised on other occasions (some with propofol) and no side effects were reported. The majority of abnormal reactions recorded were only *associated* with the use of propofol. In most instances it was one of a combination of drugs used. In only two of the 12 cases reported (1.35% of the total anaesthetised in the two month period) could a definite link be made with propofol since no other agents were given.

We suggest that the phenomena encountered may be explained in one or more of the following ways: (1) Some or all of the abnormal reactions recorded are due to the effects of propofol or its metabolites on the central nervous system or elsewhere. (2) They are associated with the drugs used for premedication when these agents are combined with propofol. Some of the results of our record analysis are very suggestive of this, since many of the reactions were recorded in cases where propofol induction followed premedication with acepromazine and methadone. They were less frequent in animals which received no premedication. (3) The side effects are related to pre-existing pathology in the animals concerned, with the threshold for the manifestation of this pathology being lowered by the drug used (in this case propofol). (4) The reactions are due to pre-existing pathology and are totally unrelated to the agents given. This is fairly unlikely in the majority of cases since some animals were anaesthetised on other occasions with other drug combinations and no untoward phenomena were reported.

Even from this limited review of the anaesthetic records our observations suggest that, in dogs, as in man, there may be an association between excitatory side effects and propofol anaesthesia. Obviously, more work needs to be done to establish the role, if any, of propofol in excitatory responses and to elucidate the mechanisms involved.

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Hazard with the Penlon AM 700 anaesthetic machine

I would like to report a potential hazard associated with a crack in the tubing leading from the patient end to the antihypoxic control (AHC) device on the Penlon AM700 anaesthetic machine. This tubing is made of plastic and is attached to the patient end of the breathing circuit and leads directly to the oxygen analyser.

A 38-year-old patient having a routine partial thyroidectomy was connected to the anaesthetic machine and her lungs artificially ventilated via a circle-system using a Nuffield 400 ventilator. The latter is a bag-in-the bottle gas-driven ventilator which can be used via a circle-system with a soda-line absorber. A routine pre-operative check of the machine failed to reveal any obvious problems. Ten minutes into the operation, the antihypoxic control system started alarming. This automatically cuts off nitrous oxide delivery to the patient and delivers 100% O_2 without stopping ventilation. A total fresh gas flow of 3 litres was in use at this time, 2 litres of nitrous oxide and 1 litre of oxygen. Before the alarm went off, the AHC indicated an inspired oxygen concentration of 34%. When the AHC started alarming it was reading 22%. The nitrous oxide was switched off and the patient given 3 litres of oxygen i.e. 100%. This failed to stop the alarm, as it was still reading 22%. A visual check of the breathing sampling tube revealed a crack at the machine end on the inlet port. Taping the tube sorted out the problem. The reason why the analyser still indicated 22% O_2 despite the patient being given 100% O_2 may be explained by the fact that the analyser was actually sampling room air via the crack in the tubing.

This case once again demonstrates that despite various attempts to make the delivery of anaesthesia safe, constant vigilance is necessary at all times.

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Riddle of the persistent leak

The case below highlights an unusual cause of a significant leak from the patient breathing system intra-operatively.

A 68-year-old man suffering from a squamous cell carcinoma of the supraglottic region was scheduled for total pharyngolaryngectomy, neck dissection and jejunal loop-free graft with microvascular anastomosis. Following induction of anaesthesia with thiopentone, ventilation of the lungs by mask proved easy and suxamethonium 100 mg was given to facilitiate tracheal intubation. At laryngoscopy only the epiglottis was visible, but a 6.5 mm disposable cuffed tracheal tube was successfully railroaded over a gum elastic bougie. Attempted wide bore nasogastric intubation using Magill intubating forceps proved more difficult due to tumour spread and oedema of the laryngopharynx. A decision not to persist was made and the nasogastric tube was left in the pharynx, with its tip thought to be at the laryngopharynx.

The patient breathed spontaneously 66% nitrous oxide in oxygen and isoflurane 1.5% whilst invasive monitoring lines were inserted. After transfer into the operating theatre an atracurium infusion was established and controlled ventilation was commenced manually using a total fresh gas flow of 7.5 litres/minute. On connecting the patient to a circle breathing system driven by a Manley Servovent and reducing the fresh gas flow to 1.7 litres/minute, the expired tidal volume was noted to be approximately 250 ml lower than the preset tidal volume. In addition, the ventilator reservoir bag was collapsed, and it became evidence that there was a significant leak from the system. Although a ventilator alarm was connected and set to alarm at 5 cmH_2O above or below the peak inspiratory pressure, it was not activated. All circuit connections were checked and found to be secure. An occasional leak was audible at the mouth and some extra air was added to the cuff of the tracheal tube as the pilot balloon did not seem well inflated. The audible leak became more pronounced and the patient's trachea was re-intubated after passing a bougie down the existing tracheal tube. However, the problem persisted and it became apparent that the source of the leak was the unspigotted nasogastric tube, whose tip was lying in the trachea. Repositioning of the nasogastric tube resolved the situation.

It is well known that fine bore feeding catheters may enter the lungs, but it is salutary to remember that even wide bore nasogastric tubes may be passed beyond the cuff of a tracheal tube. This case illustrates how such a misplaced nasogastric tube may interfere with lung ventilation. It is especially useful to remember this complication when a nasogastric tube cannot be placed under direct vision. In addition, leaks between the breathing system and the patient are much more reliably detached by expired volume monitoring than by a ventilator alarm.[1]

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Reference

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Intermittent obstruction of tracheal tube revealed during pressure-supported ventilation

Pressure-supported ventilation is a spontaneous breathing mode commonly used in the process of weaning patients from ventilatory support. Using the Servo 900C model (Siemans), the patient triggers respiration and inspiratory support at a preset constant pressure is delivered. The pressure in inspiration, therefore, never exceeds the preset inspiratory level plus any positive end expiratory pressure (PEEP) that has been added to the system. In expiration the pressure drops to zero or the preset PEEP level. Cycling from inspiration to expiration occurs when the inspiratory flow drops to less that 25% of the peak inspiratory flow (PIF).

A 62-year-old woman was admitted to the intensive care unit following a respiratory arrest. At resuscitation her trachea had been easily intubated using a size 8.0 mm cuffed tracheal tube (Portex). She had a history of bilateral pulmonary tuberculosis (TB), and treatment had included a left thoracoplasty in 1952; subsequently she developed a severe kyphoscoliosis. This, combined with restrictive parenchymal disease secondary to her TB, led to the development of cor pulmonale. An exacerbation of this had contributed to her admission. During continuous mandatory ventilation, and with the original Portex tube *in situ,* venilation had been uneventful. In the pressure support mode however, her unusual anatomy resulted in the tube abutting on the trachea and intermittently obstructing when her neck was flexed (Fig. 1). In inspiration the almost immediate drop to less than 25% of PIF resulted in premature cycling to expiration. In this state the patient generated tidal volumes of 80–100 ml at rates of 60–100 breaths per minute. Progressive hypoxia and hypercarbia ensued, and the expired minute volume alarm sounded continuously. This problem only became evident when the patient adopted a more comfortable

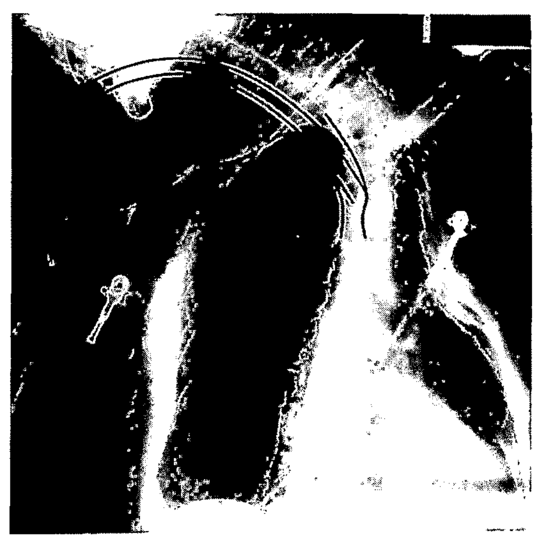

Fig. 1.

position for spontaneous respiration, whereby increased neck flexion resulted in the tube obstructing the trachea. When her neck was extended, the obstruction was relieved (Fig. 2). Use of a soft collar to prevent neck flexion was of no benefit, but the problem was easily corrected by changing the Portex to a RAE type tube with a Murphy eye.

This patient posed a long-term weaning problem. Eleven days after admission she had an elective tracheostomy. As the tracheostomy tube was shorter and more centrally placed there were no problems with pressure-supported

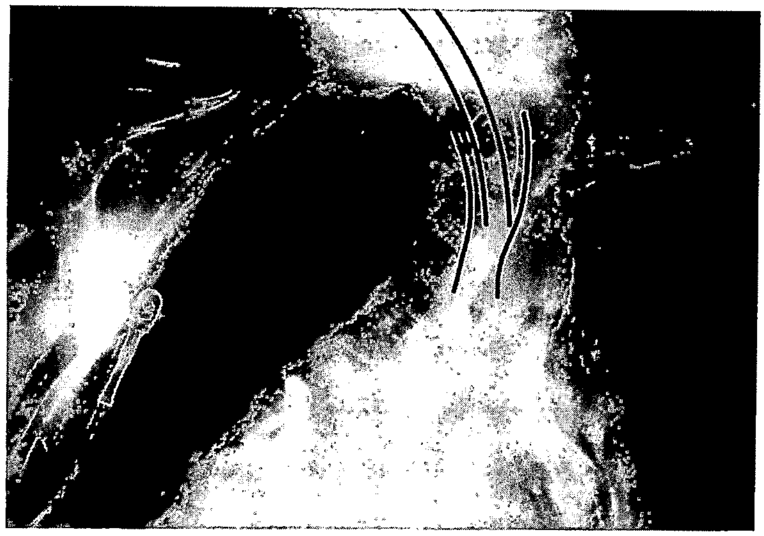

Fig. 2.

ventilation. We noted the potential for problems, because all tracheostomy tubes in our hospital are without a Murphy eye, and it is impossible to fashion one due to the distal position of the cuff. In retrospect, an early tracheostomy may have been more beneficial to the patient, allowing a smoother course of weaning.

This case clearly demonstrates the very real problem of physical obstruction of a tracheal tube by the trachea, and the benefit of a Murphy eye in such cases. It also served to remind us of the cycling features of pressure supported ventilation with the Servo 900C ventilator.

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Another set of twins

The ideal way to compare anaesthetic techniques would be to administer them to the same individual consecutively on a list. As this is not feasible, an alternative is administration to identical twins if they present together on a list, as was reported recently (*Anaesthesia* 1990; **45:** 69).

I too was presented with identical twin girls, 3 years old, who both had trigger thumbs on their left hands. They weighed 13.4 kg and 13.7 kg respectively and were fit and well. They attended for day case surgery. The ward staff assisted me in offering a modestly different anaesthetic technique to each by arbitrarily giving only the first twin premedication, although it was prescribed for both. This was trimeprazine 3 mg/kg orally, following which she arrived drowsy in the anaesthetic room. She accepted a nitrous oxide/oxygen/halothane induction via a facemask and Ayres T piece. These agents were continued for maintenance of anaesthesia. The 15 minutes operation was carried out under a tourniquet. The second, unpremedicated, twin arrived wide awake. EMLA cream had been applied to the dorsum of her right hand into which a 25G 'Butterfly' was inserted. Anaesthesia was induced with thiopentone 100 mg 2.5% and maintained with nitrous oxide/oxygen/halothane. Her operation lasted 20 minutes. Anaesthesia was uneventful. Both woke up within a few minutes and were monitored with ECG, NIBP and pulse oximeter.

The ward staff noted that the twin who had received premedication was drowsier than her sister postoperatively, but both were able to eat and drink an hour later and went home after a further hour. Neither required postoperative analgesia. Fortunately I experienced nothing so dramatic as the suxamethonium apnoea encountered in one of a pair of identical twins,[1] but I enjoyed varying the anaesthetic within the bounds of relatively minor surgery. It would be interesting to hear about identical twins receiving different anaesthetic techniques for major surgery.

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Reference

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Long distance transport of the critically ill

The recent upsurge of interest in regional intensive care[1] has prompted an evaluation of the equipment most suited to transfer of critically ill patients, as reported recently by Drs Ramage, Kee and Bristow (*Anaesthesia* 1991; **46:** 395–7). We applaud their efforts to improve equipment for mobile intensive care, but report here a case which illustrates the capabilities of more modest technologies when a specialist team prepares the patient adequately for transport and monitors invasively during it.

A 26-year-old man was admitted to hospital in Stranraer with respiratory failure. His past history included a bone-marrow transplant for acute lymphoblastic leukaemia. Chronic graft-versus-host-disease followed with subsequent obliterative brochiolitis, postirradiation pulmonary fibrosis

and recurrent infection. On admission, tracheal intubation and mechanical ventilation were instituted, but he became hypotensive and oliguric overnight and transfer to Glasgow by road was arranged the following day (day 1). On arrival in Stranraer, the secondary transport team inserted arterial and central venous cannulae. Two litres of colloid restored arterial blood pressure and urine output and arterial blood gases were satisfactory whilst he was attached to a Drager Oxylog ventilator (supplied by size E and G oxygen cylinders). Monitoring and ventilation were continued during the uneventful journey of 90 miles, which lasted 2 hours.

Following admission to the intensive care unit (ICU) in Glasgow, his trachea was extubated on day 12 and he was transferred to a respiratory ward in the same hospital on day 14. Severe bronchospasm led to re-admission and ventilation on day 28 and weaning was successfully achieved only by allowing ventilation by nasal mask at night. He again returned to the respiratory ward, but was re-admitted on day 58 with a left tension pneumothorax and hypoxic cardiac arrest. His trachea was extubated after 11 days and he was transferred from Glasgow to Newcastle 2 days later for assessment for a single lung transplant. In view of the risk of pneumothorax at altitude, he travelled by ambulance with the secondary transport team, a distance of 160 miles, taking 3 hours 50 minutes. Monitoring was by intermittent pulse oximetry and he breathed spontaneously, using the nasal ventilator intermittently. Full resuscitation equipment, including defibrillator and chest drains, was to hand.

He later returned by ambulance to the respiratory wards in Glasgow, but on day 98 was admitted for the fourth time to the ICU because of deteriorating respiratory function. He remained there, his lungs being mechanically ventilated, until day 170 when a donor lung became available; he was transferred to Newcastle that evening by the transport team in a Loganair Islander aircraft. Monitoring included direct arterial pressure, continuous ECG and pulse oximetry. The flight of 150 miles lasted 1 hour 25 minutes and transplantation of a single left lung began within 6 hours of take-off from Glasgow. The patient was breathing spontaneously on the second postoperative day and his trachea was extubated on the sixth. He was discharged home 33 weeks after his initial presentation in Stranraer, but died 6 months later of progressive disease in the nontransplanted lung.

This report illustrates the safety of secondary transport when performed by specialist teams, despite the limitations of inexpensive and widely available equipment. If there is adequate preparation before and continued monitoring during transport, the sickest patients can be safely moved over long distances to receive the most complex therapies.

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Reference

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Inadvertent submucosal penetration with a minitracheostomy cannula inserted by the Seldinger technique

Minitracheostomy was initially developed for removal of excessive secretions from the trachea and bronchi,[1] but it has also been used as an emergency airway.[2] Several complications with the percutaneous insertion of such cannulae have been described.[3-5] We report here a case in which a minitracheostomy tube advanced percutaneously into the trachea over a guide wire[6] resulted in submucosal cannulation and subsequent subcutaneous emphysema in the neck.

A 76-year-old patient was operated on because of imminent gangrene of the foot. The first night following surgery, bronchial lavage was performed because of excessive bronchial secretions. On the first postoperative morning, a minitracheostomy was considered indicated. A Mini-Trach II — Seldinger (Portex Ltd., England) was inserted percutaneously according to the manufacturer's instructions. The cricothyroid membrane was punctured with a 2 cm long 16 G Tuohy needle included in the kit. Proper position was verified by aspirating air into a saline-filled syringe. A guide wire with a soft tip was then passed into the trachea through the needle. After removing the needle, a 7-cm long curved dilator was threaded over the wire into the trachea and an introducer, with the minitracheostomy cannula over it, threaded over the wire into the trachea; the wire and the introducer were then removed. As airflow through the cannula was not felt, nor an end-tidal carbon dioxide tracing obtained, fibreoptic bronchoscopy was performed, which showed the tip of the cannula under the mucosa of the posterior tracheal wall. The cannula was withdrawn under visual control and was guided to an acceptable position, with a suction catheter advanced through the tube into the trachea. After this an adequare end-tidal carbon dioxide tracing could be recorded.

A chest radiograph taken after bronchoscopy did not show any mediastinal air. Two hours later, subcutaneous emphysema was noted on the left side of the patient's neck. No clinical signs of respiratory insufficiency were noted. The patient was closely observed and the next day he underwent re-operation under continuous spinal anaesthesia. A further bronchofibreoscopy was performed on the third day after cannulation and revealed hyperaemia at the site of the mucosal penetration on the posterior tracheal wall. The subcutaneous emphysema in the neck had resolved.

Paratracheal cannulation or oesophageal perforation are reported complications of minitracheostomy.[3-5] The position of the cannula should therefore be verified before suctioning or supplying oxygen through it. We have found that a reliable method to verify the intratracheal position of the cannula is fibreoptic bronchoscopy.[3] In the case reported here, fibreoptic bronchoscopy was performed because of absence of airflow through the tube with no end-tidal carbon dioxide trace. To avoid accidental paratracheal cannulation, the use of the Seldinger technique has been recommended.[6] In the kit used here, a straight guide wire with a flexible tip is included. The lumen of the Tuohy needle in the kit is small enough to prevent free movement of the wire through it, therefore considerable strength was needed to advance the wire. Possible resistance by the posterior wall of the trachea could not be felt and the wire was passed under the mucosa of the posterior tracheal wall. With a J-wire, the complication described here may not have been encountered.

Minitracheostomy is beneficial in the removal of excessive secretions from airway in patients with impaired ability to cough. The technique of insertion should be, however, further improved to avoid complications. Attention should be paid on adequate verification of the proper position of the cannula even after easy insertion.

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Skiers neck: an unusual cause of difficult intubation

We wish to report an unusual cause of unexpected difficult intubation.

A previously fit 49-year-old man was admitted for elective laparoscopic cholecystectomy. Pre-operative assessment was unremarkable. He had undergone an uncomplicated tonsillectomy at the age of 5 years but had received no other general anaesthetics. Premedication was with 3 mg lorazepam. Anaesthesia was induced with 200 mg propofol and 40 mg atracurium, and maintained with isoflurane and 30% oxygen in nitrous oxide. Mask ventilation was easy to perform, but at laryngoscopy the cords were impossible to visualize. Initial attempts at intubation using a gum elastic bougie and a fibreoptic laryngoscope (by an experienced operator) were unsuccessful, although intubation was eventually achieved by railroading a smaller (7.0 mm) tracheal tube over a bougie. This procedure took over 90 min. Palpation of the neck and fibreoptic laryngoscopy indicated that the larynx was not in the midline. The remainder of surgery, anaesthesia and recovery was uneventful. The patient was interviewed postoperatively, but denied any history of undue throat or chest problems.

Investigations to find a cause of the problems were undertaken; these included X rays of the cervical spine and soft tissues of the neck, and a CT scan of the laryngeal region. These showed a shift of the entire larynx to the right side together with an old fracture (with non-union) of the thyroid cartilage and some narrowing of the larynx.

It was only at routine follow up that the patient and his wife offered an explanation for the fractured larynx which they had otherwise forgotten. Some years before, the patient had sustained an injury on a skiing holiday in which he had fallen forwards, planting his ski pole in front of him. He continued to fall onto the pole, his neck being the first point of contact with the end of the handgrip. The pole was bent double by this manoeuvre. Somewhat surprisingly, the patient complained of only a slight soreness of his neck for a few hours, and continued skiiing immediately. Even more surprisingly, he has noticed no change in his voice, despite being an amateur chorister. While the force required to cause such damage to the ski pole has not been calculated, it would seem reasonable to assume it was sufficient to cause the laryngeal deformity seen during this anaesthetic.

The absence of symptoms with this type of injury is unusual, but now the winter migration to the Alpine resorts is over, perhaps the prudent anaesthetist will add a 'sports injury' section of questions to the pre-operative assessment.

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A technique to avoid dural puncture by the epidural catheter

Combined subarachnoid and epidural blocks are becoming a popular technique in obstetric anaesthesia. Concern has been expressed by obstetric anaesthetists at the potential risk of insertion of the epidural catheter into the subarachnoid space through the dural puncture site made by the spinal needle during a single-segment combined approach. The possibility of this occurrence may be greatly reduced by the following technique as described by Rawal.[1] The epidural space is identified using a Tuohy needle with the Huber point in a caudad direction and the spinal needle is introduced. The characteristics of the Huber point result in the spinal needle being angled away from the tip of the Tuohy needle before the dura is punctured. After the subarachnoid injection of local anaesthetic agent is complete the spinal needle is withdrawn, the epidural needle gently rotated 180° and the epidural catheter introduced in a cephalad direction. Using this technique of rotating the Tuohy needle one avoids exposing the tip of the epidural catheter during its insertion to the dural puncture site made by the spinal needle.

The consequences of accidently passing the catheter into the subarachnoid space may be disastrous. Although the rotation of the Tuohy needle may increase the possibility of dural puncture we believe the advantages of the aforementioned technique outweigh its disadvantages.

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Reference

1. RAWAL N. Single segment combined subarachnoid and epidural block for Caesarian section. *Canadian Anaesthetists' Society Journal* 1986; **33:** 254–5.

Attenuation of suxamethonium myalgias

We read with interest the article by Mingus *et al.* (*Anaesthesia* 1990: **45:** 834–7) concerning suxamethonium myalgia in patients following laparoscopy. It was particularly interesting to read that they found no difference between the incidence of postoperative myalgia in the patients who received suxamethonium and those who received vecuronium. As part of a wider study of post-operative complications following day case laparoscopy, we also studied patients who received either suxamethonium or vecuronium. We found that there was such a profound difference in the incidence of myalgia that we have abandoned the use of suxamethonium in these patients.

The patients we studied were allocated randomly to receive either vecuronium 4 mg or suxamethonium 75 mg followed by supplementary doses as required. They otherwise received similar anaesthetics: no premedication, induction with propofol followed by the muscle relaxant and tracheal intubation. Anaesthesia was maintained with 1% isoflurane in 33% oxygen and 66% nitrous oxide. The severity of a number of complications were assessed up to discharge and up to 24 hours after discharge by questionnaire. The patients were asked to describe their symptoms as absent, slight or severe. The symptoms inquired about included pain in shoulders, muscle pains and muscle stiffness. The incidence of these symptoms up to 24 hours after discharge are shown in the Table. It can be seen that there is no significant difference in the incidence of shoulder pain, but a significant difference in the incidence and severity of both muscle stiffness and pain is apparent.

Shoulder pain is common in patients following laparoscopy,[1] most probably due to diaphragmatic stretching and irritation caused by the CO_2 used to distend the abdomen. Mingus and colleagues comment on the fact that these pains may mask the myalgia produced by suxamethionium. They did not ask specifically about pain in the shoulders and these pains were probably classified as myalgia. In the two other studies[2,3] referred to by Mingus and colleagues as showing similar results to theirs, it must be noted that those patients who received suxamethionium were pretreated with tubocurarine. In our study we found that almost all the patients complained of shoulder pain. However, there was a significant difference in the number of patients suffering from myalgia after receiving suxamethonium compared to those receiving vecuronium. Therefore, we believe, that had Mingus and colleagues asked separately about shoulder pain and muscle pains, they may well have revealed the suxamethonium-induced myalgia demonstrated in our study. In addition, differences produced by the three pretreatments given to the patients receiving suxamethonium may have been revealed.

Table 1.

	Suxamethonium ($n = 14$)	Vecuronium ($n = 26$)
Pain in shoulders		
mild	35.7%	34.6%
severe	64.3%	42.3%
Muscle pains*		
mild	28.6%	30.8%
severe	64.3%	3.8%
Muscle stiffness*		
mild	28.6%	38.5%
severe	64.3%	0

*$p < 0.01$.

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2. Zahl K, Appelbaum JL. Muscle pain occurs after outpatient laparoscopy despite the substitution of vecuronium for succinylcholine. *Anaesthesiology* 1989; **70:** 401–11.
3. Kenefick JP, Leader A, Maltby JR, Taylor PJ. Laparoscopy: blood gas values and minor sequelae associated with three techniques based on isoflurane. *British Journal of Anaesthesia* 1989; **59:** 189–94.

Anaesthesia, 1991, Volume 46, pages 804–807

Book reviews

Problems in respiratory care, Vol. 3, No. 3; the respiratory muscles

Edited by M.J. Tobin. Pp. xi + 546. J.B. Lippincott, 1990. $27.

This book is one of a series entitled *Problems in respiratory care* and contains 16 chapters which review different aspects of respiratory muscle activity. The contributors are all specialists in their field and are drawn from the USA, Canada and Europe.

The book is probably directed mainly towards the chest physician and respiratory intensivist but should also be of interest to anaesthetists, neurologists, rehabilitation specialists and respiratory therapists. It is clinically orientated and covers many important and controversial topics. The first chapter describes briefly the anatomy and physiology of the respiratory muscles relevant to the subsequent chapters. This is followed by an excellent review of the function of the upper airway muscles. Although this information is mainly of importance in the study of obstructive sleep apnoea and little is mentioned of anaesthesia, it is very relevant to the anesthetist. The next two chapters deal with the assessment of respiratory muscle function. One outlines the clinical and laboratory tests which can be performed to measure muscle strength and the second has a balanced discussion on respiratory muscle fatigue. I particularly liked the chapter on respiratory muscle involvement in tetraplegia which is clearly presented and a model analysis of chest wall mechanics. Three chapters cover respiratory muscle function in COPD and asthma, skeletal deformity and neurological disease. There are also useful chapters on nutrition, weaning and dyspnoea.

Specific muscle treatment is discussed in chapters on rehabilitation, muscle training, pharmacotherapy, diaphragm stimulation and muscle rest. They are all informative but may be not as strong as the other chapters, perhaps reflecting the science and evidence which is not as soundly based.

The book is in hard back. The text of each chapter is divided into headings and subheadings with a summary at the end and accompanied by clear line drawings and diagrams. The references on the whole are excellent and up-to-date and sited at the end of each chapter. There is a brief but adequate index.

I would recommend this volume to any anaesthetist since we should all be interested in breathing muscles, and those interested in intensive care should find it especially relevant since the trend is more and more to encourage ventilatory assistance rather than full control.

L. Loh

Ambulatory anaesthesia

Edited by I.D. Klepper, L.D. Sanders and M. Rosen. Pp. xi + 297. Blackwell Scientific, 1991. £39.50.

With the recent expansion of day surgery this book is a timely publication. There are 24 chapters written mainly by anaesthetists, pharmacologists and psychologists. The book should have wide appeal for anaesthetists sitting their College examinations and it may well stimulate closer collaboration between basic scientists and anaesthetists researching their patient recovery. Certainly the references are pertinent and although there are a few tables and figures these are well produced.

The book is divided into five sections. In the first, anaesthetists are advised not to discharge their patients into the community under the influence of anaesthetic agents. The analogy of alcohol and its subeffects is appropriate. Perhaps a written, pre-operative statement of warning should be signed by each day patient and held in their notes. Although there is a battery of postanaesthetic impairment tests, Herbert, a psychologist, concedes that assessment of postanaesthetic mental function is far from simple.

Section 2 outlines the methods of assessing recovery. The chapter on saccadic eye movements indicates that here is a rapid, objective psychometric test which allows the effects of sedative drugs to be reliably quantified. Anaesthetists are reminded by Professor Millar, Glasgow, of the pitfalls in memory function assessment. He concedes that memory for new facts may be suppressed following general anaesthesia but he suggests that researchers will need to identify whether their tests are testing explicit or implicit memory. Furthermore, sample size is important and investigators should always include the confidence intervals of their mean values. Section 3 is an account of patient impairment following hypnotic and anaesthetic agents with reference to the elderly and paediatric patients. An occupational physician also considers the problems of testing driving performance and stresses that anaesthetists should ask their day cases, in some detail, about their occupations. The problems involving the use of benzodiazepines, opioids, intravenous and inhalational anaesthetic agents are fully discussed

in section 4. All authors agree that there is as yet no simple recovery test which is suitable for every occasion. Two experienced researchers, Sear and Dundee indicate in section 5 how to overcome the problems of recovery assessment within a busy recovery unit. The reader is instructed on the concept of a minimum infusion rate and the need for simultaneous pharmokinetic studies and recovery testing is reinforced.

Much work still remains to be done on patient recovery. However, the editors are to be congratulated for producing such a readable and thoughtful text. Anaesthetists of all grades should find this book interesting whether from an examination, clinical or research viewpoint. The book should be available in all medical school and anaesthetic department libraries. It is thoroughly recommended.

T.W. Ogg

Handbook of obstetric anaesthesia

A.S. Buchan and G.H. Sharwood-Smith. Pp. 119. W.B. Saunders, 1991. £9.95.

This pocket sized publication is based on an obstetric anaesthetic manual produced for the Royal Infirmary, Edinburgh. It is divided into nine chapters covering physiology, analgesia, anaesthesia, complications of pregnancy, haemorrhage and adult and neonatal resuscitation. Each chapter is referenced with pertinent selected papers or chapters from major texts.

The book is designed to be used as a quick revision source for candidates taking postgraduate anaesthetic examinations, for the occasional obstetric anaesthetist and for obstetricians and midwives. It serves this function by being written cogently with lists, tables, flow diagrams, illustrations and a long series of appendices. There is no chance to expand on controversial topics in this text.

Certain sections of the book will require revision. The publication date almost coincides with the latest maternal mortality report so that parts of the book need updating. Treatment of malignant hyperthermia occupies one fifth of the resuscitation section and does not reflect current opinion or the presence of a fetus *in utero*. Prophylactic management for susceptible women may have been more useful. Sickle cell disease has no mention in the book.

These problems can all be eliminated in a future edition, but until that occurs the practical information packed into this small volume will be hugely appreciated by trainers and trainees alike. A copy on the labour ward will complement individual obstetric anaesthetic protocols, and encourage obstetricians and midwives to read it.

A. Holdcroft

Emergency drug therapy

Edited by W.G. Barsan, M.S. Jastremski and S.A. Syverud. Pp. xv+655. W.B. Saunders, 1991. £44.

This multi-author text, with 30 contributors, maintains a remarkably uniform style. In the preface, a valuable point is made, namely that the choice of drug therapy is usually not difficult for most common emergencies. However, problems may arise when treating conditions that are not common, or common conditions in patients who have unusual characteristics (for example pregnancy or liver failure), and also when standard therapy does not have the expected or desired therapeutic effect. It is in these situations that the contributors have aimed to give advice and solid guidelines. On the whole they have succeeded admirably.

All chapters are short and easy to work through, with very little wasted space. The first chapter, on basic clinical pharmacokinetics, covers a lot of difficult ground concisely and in an interesting fashion. The second chapter, dealing with routes of drug administration, is contemporary and considers some points of very practical importance, such as the effectiveness of peripheral versus central administration of drugs in a cardiac arrest patient. The tracheal administration of naloxone on the opiate overdose patient, an option not commonly used in the UK, is reviewed.

Most of the remaining chapters discuss the use of emergency drugs, classified by therapeutic purpose (as in the *British National Formulary*). The book's index allows the reader to reach rapidly the excellent flow diagrams and grey boxed advice for particular clinical conditions. The book would certainly be of immense practical use in the Accident and Emergency department or Intensive Care Unit, for reference use at the patient's side if necessary. There is an excellent chapter covering the use of therapeutic gases which includes flow diagrams for the treatment of gas gangrene, air embolism and carbon monoxide poisoning and the role of hyperbaric oxygen in these clinical conditions. The use of Heliox (80% helium: 20% oxygen) in upper respiratory obstruction of nontraumatic origin is well described.

I have few criticisms of the book, save that there are some drugs in common usage in the UK which are not mentioned. An example would be the use of parenteral diclofenac (Voltarol) in the management of ureteric colic, a condition for which the book recommends the North American equivalent of pethidine. The classification of hypovolaemic shock (compensated, decompensated and end-stage) is clinically not very useful. The convention used in the Advanced Trauma Life Support (ATLS) course is better, but both ATLS and this text ignore the possibility of using degraded gelatin solutions in hypovolaemic shock. Similarly, albumin and fresh frozen plasma are dismissed as being too expensive or too hazardous. The text does acknowledge that the debate on the use of colloid versus crystalloid is nowhere nearer being solved, but a rather one-sided approach is taken.

In spite of the small number of transatlantic incompatibilities which the UK reader may encounter, I would recommend this book as a library text for all Accident and Emergency departments and Intensive Care Units. Its format allows for rapid location of essential information, and the book, at £44.00, represents good value for money.

R.A. Cocks

Trauma, anesthesia and intensive care

Edited by L.M. Capon, S.M. Miller and H. Turndorf. Pp. xvii+884. J.B. Lippincott, 1990. $125.

This large, hard-backed book describes and comments on the current management of trauma specifically from the anaesthetist's point of view. With the recommendations of the Royal College of Surgeons on the initiation of trauma centres and the introduction of the American College of Surgeons' training scheme in trauma care (Advanced Trauma Life Support, ATLS) into the United Kingdom, trauma management can be considered to be under the professional microscope. This book neatly bridges the gap

between the recommended guidelines and practical reality by giving an experienced review of the topic.

The book is divided into four sections. The opening chapter of the first section describes the historical, epidemiological and economic aspects of trauma management. It is based on North American data and although, at first sight, may seem of little use for us across the Atlantic, it does provide a glimpse of the development of a trauma service. The rest of this first section, comprising eight chapters, deals with the basic considerations of trauma management. This section starts with the establishment of care priorities (a long summary of the ATLS course) and proceeds through airway and haemodynamic management, oxygen transport, transfusion, coagulation abnormalities, pre-existing comprising conditions and the general principles of anaesthesia for acute major trauma. This section provides the fundamental structure for the rest of the book and although I found it useful and full of factual information, I was concerned that the assumed level of basic knowledge varied considerably from chapter to chapter. For example, in the chapter on the airway, basic procedures are not described, the authors proceed directly to the more complicated subjects, such as how to deal with patients with a full stomach, the initial assessment and management, including details of some very advanced airway techniques, and postintubation care. All of these are extremely relevant and written for the experienced anaesthetist. On the other hand, the chapter on pre-existing conditions provides a lot of simple medical knowledge and the chapter on general principles of anaesthesia, a great deal of basic pharmacology which should be well within the every day knowledge of the anaesthetist.

The second section details the management of specific injuries. It critically reviews, in 12 chapters, injuries to the major systems of the body and includes the injured child and pregnant patient. Of particular note is the chapter on cervical spine injuries which includes some excellent diagrams and X rays. I found the chapter on microvascular surgery, however, a little out of place in this section.

The third section examines the medical complications which occur following trauma and trauma surgery. This is probably the most controversial part of the whole book but the individual chapters provide an interesting and critical insight into the author's management regimens. In reading this section the differences in treatment schedules across the Atlantic are most noticeable. To make use of this extremely important section the reader must be willing and able to convert the recommendations to a United Kingdom format, an exercise well worth the time and effort. The fourth section is a simple chapter on the organisational aspects of trauma care. I found this too stylised to be of much use but it only comprises 40 pages, less than 5% of the whole publication.

The book is extremely well illustrated using a combination of diagrams, charts and photographs. It is indexed and extensively referenced, although the latter does tend to be North American biased. For a text written by 40 authors I found little repetition, but when this was present it was used as re-inforcement of an essential item. One annoying point was that figures referred to in the text always seem to be placed on the following page when there was adequate room near the reference. This disturbs the reading pattern and often loses the impact of the figure.

This book arrived on my desk on the opening day of the Gulf hostilities. I thought that it would be an excellent revision of advanced trauma life support protocols especially in relation to the proposed imminent arrival of casualties. As it happens, there was little on war trauma; the book dealt virtually exclusively with civilian trauma. Nevertheless, it is a notable text providing the anaesthetist who deals with trauma with an excellent and authoritative reference work.

D.A. ZIDEMAN

Studies of narcosis: An English translation of Charles Ernest Overton's classic German monograph

Edited by R.L. LIPNICK. Pp. vii+203. Chapman and Hall, 1991. £35.

Unlike the literary genre, there are relatively few science books which retain the capacity to be intellectually stimulating to successive generations. One reason is that a scientific treatise is based on data which became superseded and concepts which are constantly being redefined. However, anaesthesia is fortunate in having a number of texts which are glorious exceptions to the general rule. One of these is C.E. Overton's *Studies of narcosis* which has all the hallmarks of a classic text. First, despite the changed perspective of the modern reader, the ideas and hypotheses remain as challenging as they were in 1901. Second, the relevance of the studies extends beyond the area of anaesthesia on which they were primarily focused and the subtitle of the book correctly describes it as a contribution to general pharmacology.

This is also an example of a book which has been more quoted than read. However, the excuse has been that until this new publication it was only available in the original German edition. Indeed, it is not widely recognised that Overton was an Englishman, born in Cheshire, and a distant relative of Charles Darwin. When he was 17 he left England for Zurich and he completed his PhD, followed by very productive postdoctoral work, before moving to Sweden to become the Professor of Pharmacology at Lund in his early forties. The book was written while in Zurich and is not only an exposition of his hypotheses but also a summary of 8 years' experiments with both methodological details and quantitative results.

Overton is best known for his independent proposal of the hypothesis known as the Meyer-Overton rule. The 'rule' had a number of facets which are developed in the book. These were subsequently brought together by Meyer's son who in 1920 restated the original theory as follows: 'There will always occur narcosis, whenever a chemically indifferent substance infiltrates in a determined molar concentration into the cell lipoids.' It is this statement which forms the basis for many of the current efforts to elucidate the molecular mechanism of anaesthesia. Researchers continue to set up experiments to prove, disprove or redefine the hypothesis. Indeed, it has been argued that the Meyer-Overton rule is the universally accepted starting point for discussions of mechanisms of anaesthesia and it has only been the subsequent refinements and modern interpretations which have confused our understanding.

Overton's book should not just be read for its historical interest. It contains, for example, an excellent discussion on the critical distinctions between anaesthetics and narcotics which is highly relevant to the current development and increased usage of the latter group of drugs. The dichotomy between specific and non-specific agents is one of the connecting threads that keeps reappearing throughout the book. For this reason the experimental section includes data for many compounds that we would not consider to be anaesthetics at all. Such a broad pharmacological base is in marked contrast to some of the more blinkered approaches to the subject today.

In view of the fact that the phenomenon of anaesthesia is one of the main challenges in the elucidation of the neuro-

sciences, this book should be mandatory reading for anybody embarking on serious post-doctoral research in the broader field. It will also appeal to practising clinicians who have an intellectual interest in the underlying mechanisms of anaesthesia, whose beneficial effects society has come to take for granted.

M.J. Halsey

Books received

We thank the publishers for the following books, some of which may be reviewed in future issues of *Anaesthesia.*

The management of major trauma
Edited by C. Robertson and A.D. Redmond. Pp. 190. Oxford University Press, 1991. £12.95.

An introduction to cardiovascular physiology
Edited by J.R. Levick. Pp. 278. Butterworths, 1990. £14.95.

1990 The year book of critical care medicine
Edited by M.C. Rogers, M.D. and J.E. Parrillo. Pp. 338. Year Book Medical, 1990. £41.50.

Anesthetic management of difficult and routine pediatric patients, 2nd edn.
Edited by F.A. Berry. Pp. 496. Churchill Livingstone, 1991. £32.50.

Case studies in critical care medicine, 2nd edn.
Edited by R.D. Cane, B.A. Shapiro and R. Davison. Pp. xii + 444. Year Book Medical, 1990. £34.00.

Basic physics and measurement in anaesthesia, 3rd edn.
Edited by G.D. Parbrook, P.D. Davis and E.O. Parbrook. Pp. 344. Butterworth, Heinemann, 1991. £25.00.

Local anesthesia for dermatologic surgery
Edited by M.J. Auletta and R.C. Grekin. Pp. 99. Churchill Livingstone, 1991. £17.50.

Anesthetic management of difficult and routine pediatric patients, 2nd edn.
Edited by F.A. Berry. Pp. 496. Churchill Livingstone, 1990. £32.50.

Towards a new pharmacotherapy of pain
Edited by A.I. Basbaum and J.M. Besson. Pp. 457. John Wiley, 1991. £65.00.

Regional anesthesia, 2nd edn.
Edited by W. Hoerster, H. Kreuscher, H. Chr. Hiesel and M. Zenz. Pp. 300. Wolfe Publishing Limited. 1990.

Anaesthesia: Review 8
Edited by L. Kaufman. Pp. 314. Churchill Livingstone, 1991. £22.50.

Anesthesia for ambulatory surgery
Edited by B.V. Wetchler. Pp. 800. J.B. Lippincott, 1990. £75.00.

The oxygen status of arterial blood
Edited by R. Zander and F. Mertzlufft. Pp. xii + 294. Karger, 1991. £34.40.

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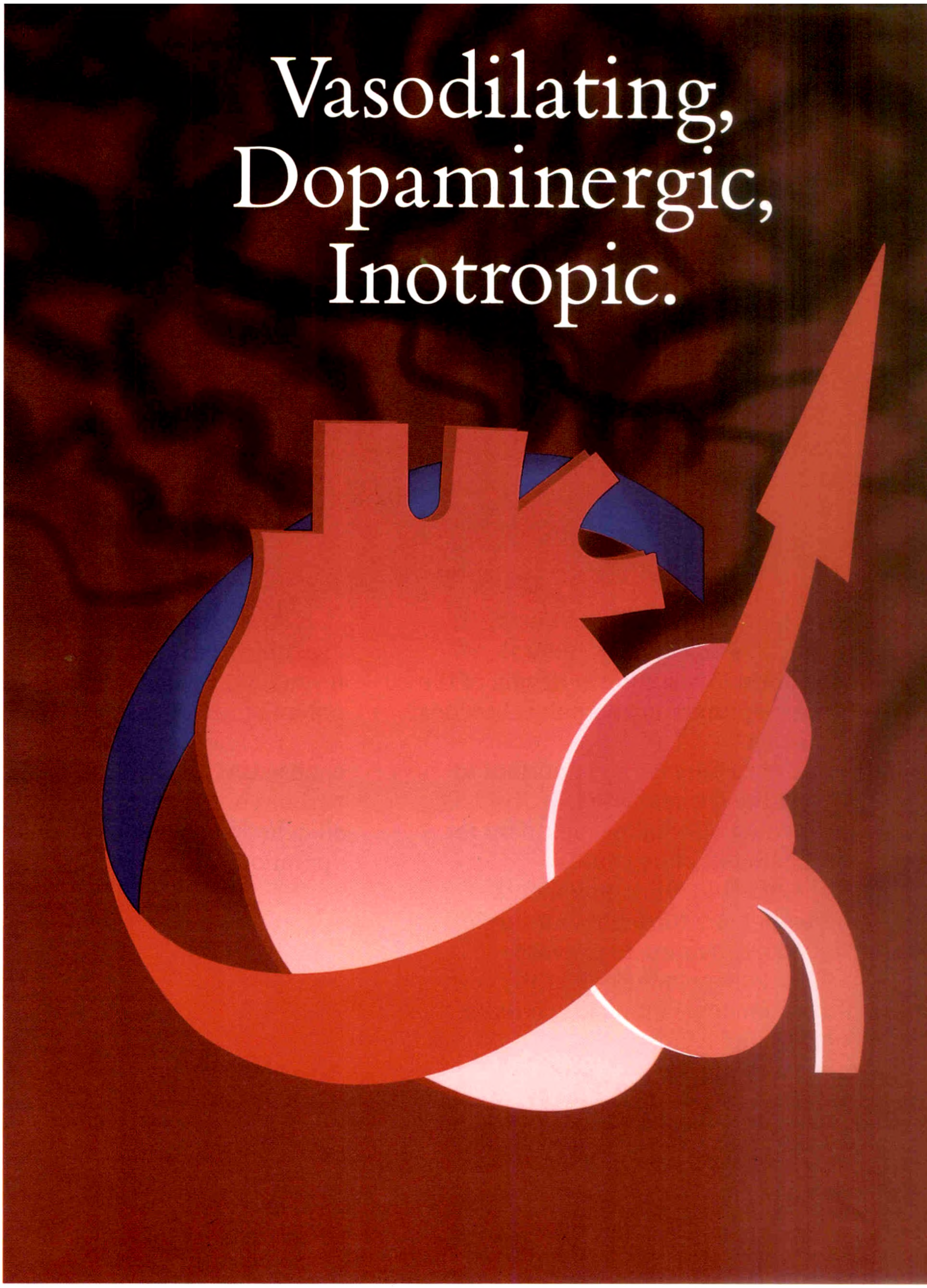

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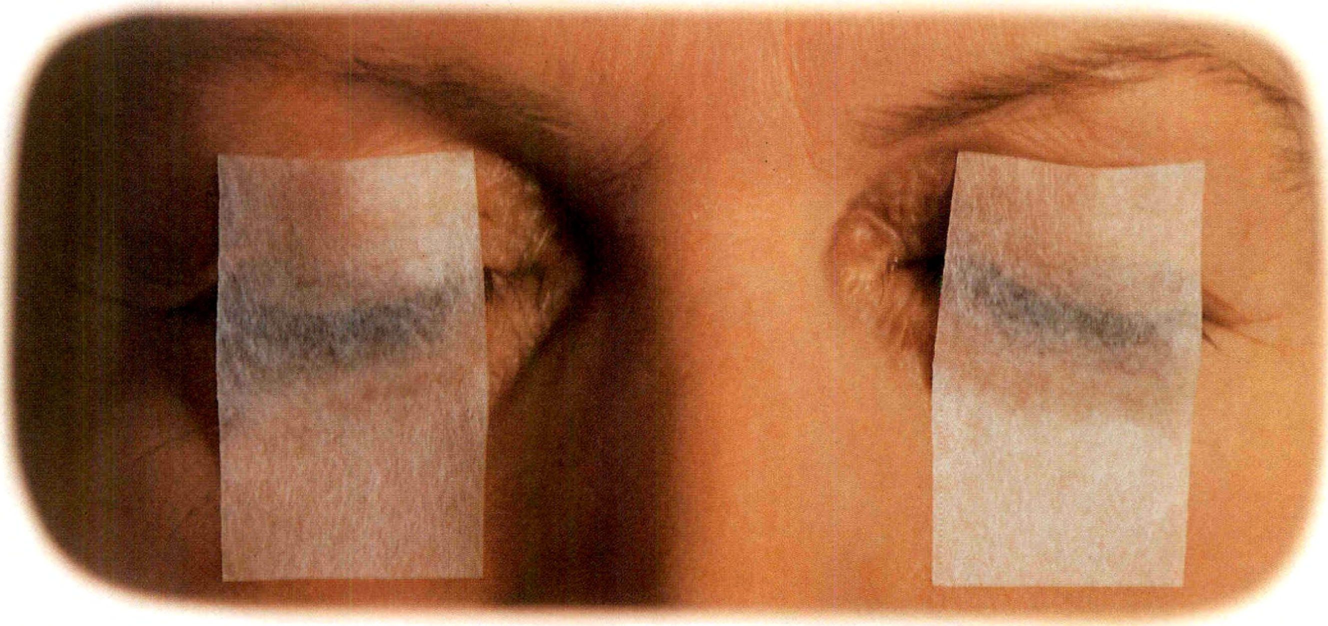

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Anaesthesia, 1991, Volume 46, pages 809

Editorial

'Alarm signals' over warning signs?

The article by Weir and Wilson in this issue of the journal (p 845) raises important issues about the safe use of anaesthetic equipment, and the effectiveness of communications on this subject between the Department of Health and anaesthetists. These are matters which are of direct concern to the Medical Devices Directorate (MDD) of the Department of Health, which is responsible for supporting the Secretary of State for Health in ensuring that medical devices and equipment for sale in the United Kingdom are safe and perform appropriately for patients and users.

Effective communication between MDD and users is vital for the safety, quality and efficacy of medical devices. It is imperative that adverse incidents arising during the use of medical devices are promptly reported to MDD for investigation, in accordance with current Departmental procedures detailed in Health Circular HC(88)51. This circular, published in 1988, is the latest in a series on the reporting of accidents in hospitals which go back as far as July 1955. To speed communication a National Reporting and Investigating Centre (NATRIC) has been set up within MDD with dedicated lines of communication for reporting adverse incidents. NATRIC can be reached by telephone on 071-636-6811 extension 3030, and by Fax on 071-436-6764. In 1990, 1147 incidents were reported by English health authorities, and a further 1338 reports were received from other sources (for example, health authorities in Scotland, Wales and Northern Ireland; manufacturers, the private health sector, the United States Federal Drug Administration and the Ministry of Defence). A wide disparity in reporting exists between Regions. West Midlands, for example, reported a total of 195 incidents whilst the numbers from Wessex and South Western Regions were 54 and 31 respectively. Interestingly, out of the 85 reports from the South West Regions, only one related to anaesthetic equipment.

During 1990, investigation of 858 reports of adverse incidents (for all categories of medical devices) showed that 15.5% were due to mechanical faults, 11.1% production faults and 5.8% quality assurance issues. Human error and incorrect use accounted for 10.4%. In 34.6% no corrective action was required by the manufacturer. Efforts to improve the safety and quality of medical devices through regulation, audit and application of standards must be backed up by adequate education and training to ensure that the device is correctly used.

The users of devices value unbiased information as a basis for informed choice when purchasing new equipment. MDD's evaluation programme covers a wide range of devices; each issue of the publication *Evaluation* contains a full report on a single product. Since November 1989, 24 reports on equipment of interest to anaesthetists have been published. The reports not only cover the technical aspects of the device (e.g. compliance with standards, laboratory performance etc.) but also give information gained by experienced users working with the device in clinical situations. These publications are issued to health authorities for local dissemination and also to hospital libraries.

MDD has developed a number of channels to communicate essential information to users of devices including Hazard Notices, Safety Action Bulletins and *Evaluation*. From time to time there are complaints about poor communication of such advice. MDD is by no means complacent about the problems of disseminating information to all who need to know, including anaesthetists. The current system relies on an established communication network at NHS Trust and district and unit level which identifies appropriate staff and ensures that they receive relevant information. These distribution arrangements need to be kept under review.

The appointment of a Safety Officer either at Health Authority, Trust or unit level could provide a focal point both for the efficient targeting and dissemination of relevant information and for communication with MDD. One health authority has already made such an appointment, perhaps others will follow this lead.

Direct mailing to anaesthetists has been proposed on several occasions. A parallel is often drawn with the issue of information from the Committee on Safety of Medicines. Superficially this may be attractive, but to target only one professional specialty would draw criticism from others, since most devices are used by staff in several specialties and occupational groups. Direct mailing of advice on device-related issues would have to be sent to all medical staff, which would result in recipients being flooded with information, most of which would not be relevant to their work. The danger would be that they would not have the time or inclination to pick out the relevant notices. Nevertheless, MDD is keen to target safety advice as effectively as possible and will continue to seek ways of doing so.

Those who read safety-related circulars will have seen the paragraph headed 'how to report defects'. This was introduced to close the communication loop and encourage reporting to MDD. Effective communication between professionals, manufacturers and MDD is essential if we are to tackle together the quality and safety issues which always present a potential threat to patients. Lines of communication should be reinforced and developed if they do not exist already. This is not a task which can ever be completed. Rather, there is a need for continuous and sustained action by all concerned to make the arrangements for communicating essential information about medical devices as effective as possible.

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0003–2409/91/100809+01 $03.00/0

Anaesthesia, 1991, Volume 46, pages 810–815

Cross-sectional study of complications of inhalational anaesthesia in 16995 patients

J. K. L. LEW, A. A. SPENCE AND R. A. ELTON

Summary

Patients undergoing anaesthesia in which halothane, enflurane or isoflurane were used, were surveyed with reference to 16 unwanted effects selected by the nominal group method. A simple record card was completed at the time of anaesthetic administration. The overall incidence of complications was 13.9%. One complication was reported in 10.8% of the cases, and more than one in 3.1%. Complications were more frequent in the obese, the elderly and those patients receiving isoflurane, but in view of the small overall use of this agent, the anaesthetists involved may still have been on a learning curve.

Key words

Anaesthetics; volatile; complications.
Anaesthesia; audit.
Nominal group technique.

The three main volatile agents in current use in Britain for inhalational anaesthesia are halothane, enflurane and isoflurane, but there is little comparative information on the relative safety of these agents and complications associated with their use. We sought to gather information on aspects of anaesthetic practice in the hospitals of South East Scotland (Edinburgh, Fife and the Borders) and on the comparative use of halothane, enflurane and isoflurane. We examined the incidence of selected complications associated with these agents.

Method

The nominal group technique, described by Delbecq, Van de Ven and Gustafson,[1] was used to designate complications associated with the use of inhalational agents. It is essentially a survey of opinions of experts, conducted along very strict guidelines, using in this case a panel of eight consultant anaesthetists, one of whom acted as chairman. The list of complications that resulted from the survey is shown in Appendix 1. Hepatitis and malignant hyperthermia were also selected by the panel but were excluded from our study because of their extreme rarity and almost certain local notoriety.

A questionnaire was designed with the aim of preserving the anonymity of the patient and the anaesthetist. Its completion was made as easy as possible, without resort to case records. The amount of information sought was minimised in the hope of ensuring good compliance from the participants. In addition to the complications already mentioned, information was sought with regard to the age and size of the patient, seniority of the anaesthetist, and anaesthetic technique. The final questionnaire (Appendix 1) was printed on cards and a series of guidelines (Appendix 2) was issued to help the anaesthetist complete it. The actual complications were not strictly defined. The participants were asked to consider a complication as an unexpected occurrence which caused concern or warranted some specific action.

Anaesthetists from 14 hospitals took part in the survey. A coordinator was appointed for each hospital or group, who had the responsibility for publicising the study, distributing the cards, collecting and returning them to us. Data collection started on 1 December 1987 and finished on 31 May 1988, a period of 6 months punctuated, as it turned out, by reduced normal operative work as a result of industrial action.

The information obtained from the cards was entered onto a computer and the data were subjected to statistical

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Accepted 14 January 1991.

0003–2409/91/100810+06 $03.00/0

Table 1. Use of volatile anaesthetic agents (%) according to age, size of patient, grade of anaesthetist, induction agent and tracheal intubation.

	Halothane	Enflurane	Isoflurane
All patients	46.6	45.4	8.0
Age			
< 10 years (11.3%)	83.5	11.4	5.1
10–60 years (67.8%)	44.4	48.0	7.6
> 60 years (21%)	33.6	55.4	11.0
Size			
Obese (8%)	42.4	50.9	6.7
Nonobese (92%)	46.9	44.9	8.2
Grade			
Registrar/Senior House Officer (30.4%)	41.5	53.0	5.5
Consultant/Senior Registrar (69.6%)	48.8	42.1	9.1
Induction agent			
Thiopentone (55.8%)	48.0	44.7	7.3
Inhalational induction (8.5%)	85.8	8.3	5.9
Other (35.7%)	34.7	55.6	9.7
Intubation			
Yes (47.7%)	45.2	43.6	11.2
No (52.3%)	47.7	47.1	5.2

analysis using the Chi-squared test and multiple logistic regression.

Results

A total of 17395 usable cards were collected; of these, 400 were discarded because of inadequate completion. Compliance was variable, but was good in the large hospitals from which most of the cards came. The four major hospitals from which 68% of the cards originated had a response rate ranging from 72% to 75%. Three of the hospitals (5% of the cards) could not provide the total for volatile anaesthetics administered over the period of the study so that their response rate could not be ascertained.

Information on anaesthetic practice (Table 1)

Age. Most of the patients (67.8%) were in the 10–60 years age group. Overall, halothane and enflurane were used equally often. Isoflurane was used in only 8% of the cases. Halothane was the most popular agent in children while enflurane was preferred in the over-60s. Isoflurane was also more often used in the latter group (11%).

Obesity. Eight percent of the patients were considered to be obese. Enflurane was used most often in this group (50.9%).

Seniority of anaesthetist. A senior anaesthetist (consultant or senior registrar) was present in 69.6% of the cases. The junior anaesthetists working alone used enflurane more often, whilst the seniors were more likely to use halothane. The latter also used isoflurane more frequently than their junior colleagues.

Anaesthetic technique. Thiopentone was the most popular induction agent, used in 55.8% of the cases. 8.5% of the patients had an inhalational induction; most of these were from the less-than-10-years age group (87%). In 85.6% of these cases, halothane was the agent used.

In 47.7% of the patients, the trachea was intubated; suxamethonium was used in 68.9% of these. Isoflurane was used more frequently in the intubated patients, 52.6% of whom had artificial ventilation of the lungs. Enflurane was used more often in the ventilated patients and halothane more often in those breathing spontaneously.

Complications

The overall incidence of complications was 13.9% (Table 2); 10.8% of the patients had one complication and 3.1% more than one; a higher incidence of one or more complications was associated with isoflurane. Several of the complications tended to occur together: bradycardia/hypotension/myocardial ischaemia, breath-holding/airway obstruction/laryngospasm/excessive airway secretions, breath-holding/difficulties in maintaining anaesthetic depth and excessive airway secretions/bronchospasm. Table 3 gives a breakdown of incidence of complications in relation to the inhalational agent.

Cardiovascular. There was an association between choice of inhalation agent and tachycardia, bradycardia, cardiac arrhythmias and arterial hypotension but not observed electrocardiogram (ECG) changes suggestive of myocardial ischaemia. A higher incidence of tachycardia and hypotension was associated with the use of isoflurane. Bradycardia was less common in the enflurane group and there were more cardiac arrhythmias in the halothane group. Overall, enflurane was associated with the least cardiovascular complications.

Table 2. Frequency (%) of occurrence of complications.

	All	Halothane	Enflurane	Isoflurane
No complication	86.1	86.7	86.6	79.3
1 complication	10.8	10.6	10.4	14.2
> 1 complication	3.1	2.7	3.0	6.5

Table 3. Incidence of complications according to volatile agent.

Complications	% of patients with complications				
	All patients	Halothane	Enflurane	Isoflurane	Significance
Tachycardia	1.1	0.8	0.9	4.7	$p < 0.001$
Bradycardia	1.8	2.1	1.4	2.5	$p < 0.001$
Arrhythmia	2.2	3.4	1.0	1.8	$p < 0.001$
Myocardial ischaemia	0.2	0.1	0.2	0.4	$p < 0.05$
Hypotension	1.8	1.2	1.9	4.1	$p < 0.001$
Airway obstruction	0.8	0.8	0.8	1.3	NS
Breath-holding	1.5	1.1	1.7	2.5	$p < 0.001$
Laryngospasm	1.2	1.1	1.0	2.9	$p < 0.001$
Bronchospasm	0.5	0.6	0.5	0.5	NS
Respiratory depression	0.5	0.3	0.5	1.3	$p < 0.001$
Secretions	1.1	0.9	1.2	1.8	NS
Vomiting and regurgitation	0.7	0.6	0.8	1.4	NS
Anaesthetic depth	2.0	0.9	2.9	3.4	$p < 0.001$
Slow recovery	1.1	1.2	0.9	1.6	$p < 0.01$
Shakes/shivers	1.9	2.0	1.7	1.8	NS
Idiosyncrasy	0.1	0.1	0.1	0.1	NS

NS, not significant.

Respiratory. The choice of inhalational agent was related to the incidence of breath-holding, laryngospasm and respiratory depression but not airway obstruction, bronchospasm and excessive secretions. Patients receiving isoflurane had more breath-holding, laryngospasm and respiratory depression.

Vomiting and regurgitation. The choice of volatile anaesthetic did not seem to relate to the incidence of this complication.

Anaesthetic depth. There was a very low incidence of problems associated with maintaining anaesthetic depth in patients having halothane (0.9%) as opposed to enflurane (2.9%) and isoflurane (3.4%).

Recovery. There was more reporting of slow recovery in the isoflurane group but the choice of inhalational agent did not show any relation to the incidence of shakes and shivers in the recovery period.

Idiosyncrasy. The occurrence of idiosyncratic reactions was 0.1% and was not associated with the choice of volatile anaesthetic.

Contribution of factors other than inhalational agent on the incidence of complications

Hospital. There was a significant difference in the level of reporting of the complications between the hospitals taking part in the study.

Age. The over-60-years age group had a higher incidence of cardiovascular complications, except for tachycardia. Bronchospasm and slow recovery were also more common in this age group. Laryngospasm occurred more commonly in the less-than-10-years age group. The highest incidence of shakes and shivers was in the 10–60-years age group.

Weight. The obese patients had more cardiovascular and respiratory problems. They were also more prone to vomiting and regurgitation and presented more difficulties with maintenance of anaesthetic depth.

Seniority of anaesthetist. There was a higher incidence of tachycardia and hypotension in those patients looked after by a senior anaesthetist, whereas the junior anaesthetists

Table 4. Multiple logistic regression analysis: significance of choice of volatile agent when adjusted for other factors.

Complications	Significance of volatile agent	Other significant factors
Tachycardia	$p < 0.001$	Hospital, grade, suxamethonium, IPPV
Bradycardia	$p < 0.001$	Hospital, age, intubation, suxamethonium
Arrhythmia	$p < 0.001$	Hospital, age, induction, suxamethonium
Myocardial ischaemia	NS	Not analysed
Hypotension	$p < 0.001$	Hospital, grade, age, intubation
Airway obstruction	NS	Not analysed
Breath-holding	$p < 0.001$	Hospital, weight, induction, suxamethonium, IPPV
Laryngospasm	$p < 0.001$	Hospital, grade, weight, induction, IPPV
Bronchospasm	NS	Not analysed
Respiratory depression	$p < 0.001$	Suxamethonium
Secretions	NS	Not analysed
Vomiting and regurgitation	NS	Not analysed
Anaesthetic depth	$p < 0.001$	Hospital, weight, induction, suxamethonium, IPPV
Slow recovery	p. < 0.01	Hospital, induction, suxamethonium, IPPV
Shakes/shivers	NS	Not analysed
Idiosyncrasy	NS	Not analysed

NS, not significant; IPPV, intermittent positive pressure ventilation.

reported laryngospasm, vomiting, regurgitation, shakes and shivers more often.

Induction method. There was a higher incidence of reporting of arrhythmias, hypotension, slow recovery and shakes/shivers in those patients receiving thiopentone. Inhalational induction was associated with a higher incidence of laryngospasm but fewer problems with anaesthetic depth.

Intubation and suxamethonium. There was a higher incidence of cardiovascular complications, bronchospasm, excessive secretions, vomiting/regurgitation, slow recovery and shakes/shivers associated with tracheal intubation compared with nonintubation. The patients given suxamethonium had a higher incidence of the same complications.

Intermittent positive pressure ventilation (IPPV). There was a higher incidence of cardiovascular complications, bronchospasm, excessive secretions, vomiting/regurgitation and slow recovery in the patients having IPPV. The patients breathing spontaneously presented more airway and anaesthetic depth problems.

Since many of the factors discussed above are interrelated, univariate analysis would not have been able to rule out the concomitant effect of the other factors when one specific complication is examined. The data were therefore subjected to multiple logistic regression analysis and the effect of the choice of inhalational agent on the incidence of the various complications was analysed when adjusted for the effects of the factors discussed above (Table 4). The selection of anaesthetic agent was seen to be highly significant in the incidence of tachycardia, bradycardia, arrhythmia, hypotension, breath-holding, laryngospasm, respiratory depression, difficulty with maintenance of anaesthetic depth and slow recovery.

Discussion

The present study is not meant to show cause–effect relationships but to point out areas which might be examined further under more controlled conditions. The findings are of particular interest in view of the large number of patients studied. There is a subjective element in the reporting of the complications and we were unable to validate the reports received or to determine the level of agreement between any two anaesthetists. This was unavoidable in view of inherent difficulties associated with defining range of values.

In the South East of Scotland, halothane and enflurane were used with approximately equal frequency over the period of the study, while isoflurane was used in only 8% of the cases. Halothane was seen to be the agent of choice in anaesthetising children. The technique of spontaneous breathing in patients with tracheal tubes was used commonly. Only 52.6% of these patients had IPPV.

The junior anaesthetists used enflurane more frequently. This might reflect their concern and anxiety regarding the publicity surrounding 'halothane associated hepatitis'.[2–5]

The more recently introduced isoflurane was associated with a higher incidence of complications. It might be argued that at the time of the study the anaesthetists were still learning how to use this agent. This has, however, been disputed in a recent study.[6] There is also the possibility that isoflurane was being used in more seriously ill patients who were more likely to have complications.

Isoflurane was associated with a higher incidence of tachycardia and hypotension; this was consistent with previous findings.[7] Some authors have shown that isoflurane may be associated with a higher incidence of regional myocardial ischaemia.[8] In our study, there was no significant difference in the incidence of myocardial ischaemia between the three volatile agents. However, it is likely that not all of the patients studied had ECG monitoring, so that diagnosis of ischaemia would not have been possible. Previous reports that more arrhythmias were associated with halothane[9] were confirmed.

Although airway obstruction and excessive secretions were more common in the isoflurane group, this was not found to be statistically significant. Isoflurane was, however, found to be associated with a significantly higher incidence of breath-holding, laryngospasm and respiratory depression ($p < 0.001$). Previous authors similarly have reported a higher incidence of airway problems with isoflurane.[6,7,10–12]

Halothane was associated with a relatively small incidence of problems with maintenance of anaesthetic depth. This may be specially relevant in patients at risk of regurgitation, in whom accidental light anaesthesia must be avoided.

Isoflurane was unexpectedly associated with a higher incidence of slow recovery. However, information was not sought with regard to premedication and use of opioids peri-operatively.

In conclusion, our study has shown that usage of volatile agents is associated with an overall 13.9% incidence of complications. Of the three agents studied, isoflurane seemed to fare less well than the other two, but this might be explained by the lack of experience in its use.

Acknowledgments

We express our gratitude to the anaesthetists and theatre nurses from the participating hospitals for their support and cooperation. We particularly acknowledge the hard work put in by the following Consultant Anaesthetists who were acting as coordinators: Drs M. R. Logan, A. Milne, G. Pugh, E. Lloyd, I. Hudson, J. L. Jenkinson, I. Davie, J. Jenkins, J. McClure, H. Anderson, R. A. Bowie, W. Brown and M. R. Milhench.

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Appendix 1

Printed card sent to all participating hospitals to be filled in by the most senior anaesthetist present.

Anaesthesia study (Tick box for **yes**)

Patient	< 10 years	1
	10–60	2
	60+	3
	overweight	4
Anaesthetic	Registrar/Senior House Officer	5
	Consultant/Senior Registrar/Other	6
Induction:	Thiopentone	7
	Inhalation	8
	Other	9
Inhalation	Halothane	10
	Enflurane	11
	Isoflurane	12
	Intubation	13
	Suxamethonium	14
	IPPV	15
Complications		
Tachycardia		16
Bradycardia		17
Arrhythmia		18
Myocardial ischaemia		19
Hypotension		20
Airway obstruction		21
Breath-holding		22
Laryngospasm		23
Bronchospasm		24
Respiratory depression		25
Secretions		26
Vomiting/regurgitation		27
Anaesthetic depth		28
Slow recovery		29
Shakes/shivers		30
Idiosyncrasy		31
None		32

Return to: Secretary,
University Department of Anaesthetics
Royal Infirmary, Edinburgh.

Appendix 2

Guidance on completing the 'Anaesthesia Study' card

Please tick the appropriate box for the age range of the patient.

Overweight means that in your clinical judgement the patient is likely to exceed expected body weight by 20% or more.

For *Grade of anaesthetist* tick box 5 if the anaesthetist (or the most senior anaesthetist) is a registrar or SHO. All others use box 6.

Induction Tick box 7 for thiopentone, box 8 for inhalational induction, box 9 for any other method of inducing anaesthesia.

Inhalation anaesthesia

Halothane	box 10
Enflurane	box 11
Isoflurane	box 12

Box 13 should be ticked if the trachea has been intubated, box 14 if suxamethonium has been given and box 15 if artificial ventilation of the lungs has been the main respiratory mode during the anaesthetic.

Complications

Tachycardia, bradycardia and *hypotension* refer to increase or decrease in heart rate or a fall in arterial pressure of a degree that *had not been expected* when the anaesthetic was commenced.

Arrhythmia refers to any abnormal cardiac rhythm, seen on ECG or palpated, which has arisen during anaesthesia. Mere continuation of an arrhythmia which was present in the pre-operative period should not be entered.

Myocardial ischaemia. This refers to changes in the ECG, which the anaesthetist considers to be representative of ischaemia, which was not manifest in the pre-operative ECG and which was not expected during anaesthesia.

Airway obstruction, breath-holding, laryngospasm, bronchospasm, respiratory depression. If these disorders are minor they should not be reported. Thus, easily corrected airway obstruction can occur as part of many 'mask' anaesthetics. Each category is considered as worth reporting when the degree of the disorder is more than usually troublesome or some significant therapeutic manoeuvre has to be undertaken. Thus, there remains a matter of judgement for each anaesthetist. For example, an edentulous elderly person might be expected to maintain a clear airway only if an oropharyngeal airway was inserted. In the case of younger patients, the anaesthetist might have anticipated being able to maintain an airway without artificial aids, but judgement on this will depend on a variety of physical factors in the patient.

Secretions refers to oropharyngeal secretions which are troublesome and much more copious than the anaesthetist had expected. The mere fact of having to aspirate secretions from the pharynx or elsewhere in the airway, in an amount that occasions no surprise, should not be entered.

Vomiting/regurgitation. This refers to the occurrence of these problems during induction, maintenance or immediate recovery from anaesthesia. It does *not* relate to vomiting or regurgitation in the period following awakening.

Anaesthetic depth. This refers to a situation, not expected by the anaesthetist at the outset of the anaesthetic, in which it is felt that the control of depth of anaesthesia is more troublesome than might have been expected. In addition to signifying a circumstance in which the concentration of an inhaled anaesthetic has to be increased, the term also includes the need to give intravenous drugs of any kind to obtain greater control of the patient's state of unconsciousness (induction agent or neuromuscular blocker).

Slow recovery refers to the patient taking longer to wake up than the anaesthetist expected.

Shakes/shivers. This refers to the occurrence of these phenomena whether the patient is unconscious or has just emerged from unconsciousness.

Idiosyncrasy denotes any response to any drug given during anaesthesia which is deemed to be qualitatively different from what was expected.

If no entry has been made in any of the boxes under 'complications' please make a tick in box 32 ('none').

Anaesthesia, 1991, Volume 46, pages 816–819

Comparison of the effects of oral nizatidine and ranitidine on gastric volume and pH in patients undergoing gynaecological laparoscopy

M. T. POPAT O. J. DYAR AND C. E. BLOGG

Summary

Ninety patients who presented for elective gynaecological laparoscopy as day cases were allocated at random to three groups and studied on a double blind basis to compare the effects of nizatidine, ranitidine or placebo on gastric secretion. All the patients received the active drugs or placebo orally at least 45 minutes before the induction of anaesthesia. After tracheal intubation gastric fluid was aspirated via an orogastric tube and the volume and pH of the aspirate were measured. Venous blood samples were obtained at the times of gastric sampling to determine the plasma levels of the drugs. The proportion of patients with both pH > 2.5 and volume < 25 ml were 100%, 90%, and 92.9% in the nizatidine, ranitidine and placebo groups respectively. There was no difference in volume between groups. Two patients in the nizatidine group without a measurable aspirate had blood levels less than the therapeutic range. The median pH values in both treated groups were significantly greater than in the placebo group, but there were no differences between the two treated groups. There were 19 (67.8%) patients in the placebo group with pH < 2.5. This was significantly higher than the 2 (7.4%) and 6 (20%) in the nizatidine and ranitidine groups respectively. When the time interval between drug administration and induction of anaesthesia was divided arbitrarily into 45–90 minutes and > 90 minutes, all the patients in the nizatidine and ranitidine groups with pH < 2.5 were given the drugs in the 45–90 minute interval; this suggests a latent period is required before the gastric pH increases. Nizatidine may be an effective protective agent against acid aspiration syndrome.

Key words

Gastrointestinal tract; pH stomach.
Histamine, H_2 receptor antagonists; nizatidine, ranitidine.

Aspiration of gastric contents is a serious cause of anaesthetic morbidity and mortality.[1] First described by Mendelson in 1946,[2] it still remains a major cause of mortality in the obstetric patient.[3] Measurable factors which influence the severity of the aspiration syndrome include the pH and volume of the gastric contents. Criteria which have been used to define patients 'at risk' of developing Mendelson's syndrome include a pH < 2.5 and volume > 25 ml (0.4 ml/kg).[4,5] Risk factors include obesity,[6,7] late pregnancy,[8,9] children,[10] and those presenting for emergency surgery.[11,12] Day case patients may be at particular risk of aspiration following regurgitation compared to a similar group of inpatients since they have significantly higher gastric volumes.[13] H_2 blockers administered before operation have been used to reduce the acidity and volume of the gastric contents and thus prevent the aspiration syndrome.

The purpose of the present study was to compare the effects of prophylactic nizatidine (N) and ranitidine (R) on gastric secretion in patients undergoing day case laparoscopy. Nizatidine is a highly selective H_2 receptor blocking drug which is as potent as ranitidine and characterised by high oral bio-availability (90%) compared to ranitidine (50%) and a short time to peak plasma levels (within 2 hours) after oral dose.[14]

Materials and methods

Ninety healthy women (ASA 1–2) presenting for elective day case gynaecological laparoscopy were studied in a double-blind randomised fashion. The study was approved by the Central Oxford Research Ethics Committee and informed consent was obtained from all patients. Any patient with a history of gastro-intestinal disease or

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surgery, obesity, who was receiving drugs likely to interfere with gastric secretion, or who was allergic to this group of drugs was not studied.

The patients were allocated at random to three groups of 30 after being starved for at least 8 hours. Group N patients received nizatidine 150 mg, group R ranitidine 150 mg and group P placebo. All drugs were presented in identical capsule form and were swallowed with a maximum of 20 ml of water at least 45 minutes before induction of anaesthesia. No other premedication was prescribed.

A 21-G cannula was inserted into a large forearm or antecubital vein. Anaesthesia was induced with propofol 2.5 mg/kg and fentanyl 1–2 μg/kg followed by either vecuronium (4–5 mg) or atracurium (15–20 mg). After manual ventilation of the lungs, the trachea was intubated and anaesthesia maintained with 67% nitrous oxide in oxygen supplemented by a volatile agent (enflurane or isoflurane) or a propofol infusion.

Immediately after tracheal intubation, a size 14 FG red rubber orogastric tube was passed into the stomach and its position checked by auscultation of injected air over the epigastrium. Gastric juice was then aspirated through the tube. A 10-ml sample of venous blood was taken for drug levels at the same time. Gastric and blood sampling were carried out every 15 minutes and at the end of the procedure before extubation. Observation was made for any evidence of gastric regurgitation or possible aspiration.

Gastric volumes were measured with a syringe; the value of pH was determined by a previously calibrated pH meter (Whatman or Corning) with a microelectrode. The pH values were also checked with close-range pH paper (Whatman). The blood samples were centrifuged and the plasma separated and stored at −20°C until drug levels were determined. Plasma concentrations of nizatidine and ranitidine were measured in the laboratories of Simbec Research Ltd by reverse phase high pressure liquid chromatography with ultraviolet detection, following extraction of the plasma with 10% propanol in dichloromethane under alkaline conditions. The sensitivities for the assays were 20 ng/ml and 5 ng/ml for nizatidine and randitidine respectively. For nizatidine, the interassay coefficient of variation at concentrations between 41.5 and 1852.8 ng/ml ranged from 9.9% to 1.9%; and the interassay coefficient of variation ranged from 8.4% to 0.5%. For ranitidine, the interassay coefficient of variation was between 5.1% and 7.0% over the concentrations range 5–79.3 ng/ml; the corresponding intra-assay coefficient of variations were between 6.3% and 1.8% at concentrations of 10–165 ng/ml.

All the patients were seen by one of the investigators before discharge and given forms in a reply paid envelope to report any side effects attributable to the drugs. Ordinal data were analysed using the ANOVA and Mann–Whitney *U* tests. Nominal data were analysed by the Chi-squared test with Yates' correction for small numbers.

Table 1. Patient data: Results are expressed as mean (SEM).

	Groups		
	N	R	P
Number of patients	27	30	28
Age; years	32 (1.2)	33 (1.0)	30.8 (1.3)
Weight; kg	61.7 (2.3)	65.7 (2.0)	67.7 (2.4)
Height; cm	162.9 (1.4)	164.1 (1.1)	163 (1.5)
Time (T); minutes	91.9 (4.9)	87.3 (4.9)	80.7 (4.7)
Range	45–147	47–183	45–140

N, nizatidine 150 mg; R, ranitidine 150 mg; P, placebo; T, time from drug administration to induction.

Results

Ninety patients were recruited into the study; five were eliminated from analysis for protocol violation. Thus, results are shown for 27 patients in group N, 30 in group R and 28 in group P. The groups were comparable with regard to age, weight, height and times from test drug administration to induction of anaesthesia (Table 1). No patient suffered any adverse effect during the conduct of anaesthesia. The volume and pH of gastric aspirates at the time of induction of anaesthesia are shown as median and ranges (Table 2). There were no significant differences between the three groups when volumes were compared ($F = 1.1386$;NS). This analysis was carried out on all values, including those patients in whom no aspirate could be obtained. When volumes were compared for only those patients from whom there was a measurable gastric aspirate, there was no significant difference between groups overall. Two patients in the N group without aspirates had plasma concentrations below the therapeutic level ($>$ 600 ng/ml)[15] but no patient in the R group without aspirates had plasma concentrations below the therapeutic level ($>$ 100 ng/ml).[16] The median pH values in both treated groups were significantly greater than in the placebo group ($F = 21.9487$; $p < 0.001$). There were no significant differences between the two treated groups.

If the patients at risk of Mendelson's syndrome are defined by pH < 2.5 and volume > 25 ml, there was none (0%) in group N, three (10%) in group R and two (7.1%) in group P (Fig. 1). There was no significant difference between groups. However, considering either factor as a potential risk of aspiration pneumonitis, there were two (7.4%) patients in group N, six (20%) in group R, and 19 (67.8%) in group P with a pH of < 2.5 at risk; (Chi-squared $= 21.280$; $p < 0.001$; N vs P; and Chi-squared $= 13.525$; $p < 0.001$; R vs P). When the groups were arbi-

Table 2. Gastric volumes and pH at induction.

	Groups		
	N	R	P
Number of patients	27	30	28
Number of patients without aspirates	15	12	8
Volume; ml, median range	0 0–16	2.5 0–90	4.5 0–30
pH, mean, range	6.35* 2.0–7.0	5.9* 1.0–7.7	1.4 0.7–6.8

N, nizatidine 150 mg; R, ranitidine 150 mg; P, placebo.
*$p < 0.001$ N vs P and R vs P.

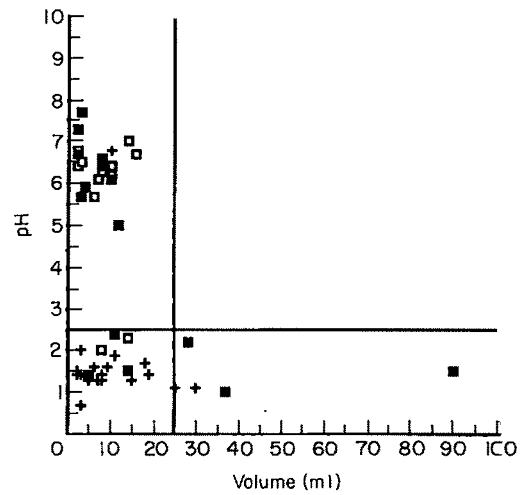

Fig. 1. Volume and pH of gastric aspirate at induction. □, nizatidine; ■, ranitidine; +, placebo.

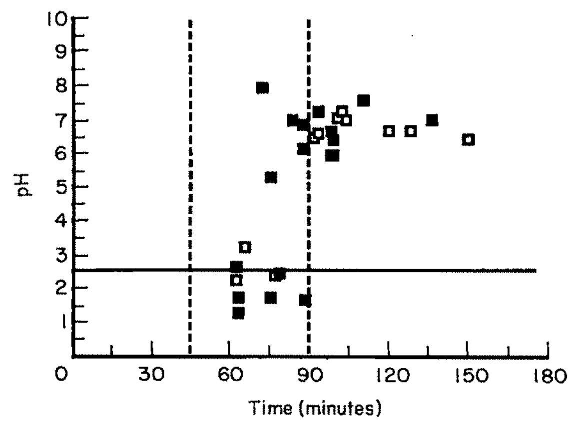

Fig. 2. Time from drug administration to induction and pH. □, nizatidine; ■, ranitidine.

trarily divided into 45–90 minute and > 90 minute drug administration-to-induction periods, all the patients in the N and R groups with a pH < 2.5 had been given the drugs between 45–90 minutes. No patient in either group had pH < 2.5 when this interval was more than 90 minutes (Fig. 2). There were no major side effects seen in the treated groups.

Discussion

The severity of aspiration pneumonitis depends on the acidity of the gastric contents.[2,5,17] Pharmacological prophylaxis for the prevention of the syndrome is directed towards elevating the pH and reducing the volume of gastric contents. Drugs which have been used include antacids, anticholinergics, metoclopramide, H_2 blockers and omeprazole.[18] Drawbacks of the use of antacids include their inability to neutralise very large volumes of acid in the stomach, short duration of action, increase in the volume of gastric contents[8,19,20] and pulmonary lesions from aspiration of antacid particles.[21–23] Metoclopramide decreases intragastric volume, but has no effect on pH.[24,25] H_2 receptor blockers reduce both basal gastric secretion and that which occurs in response to gastrin or food.[18] They are more effective than antacids in increasing intragastric pH and, unlike antacids, do not increase, and may decrease, the volume of gastric fluid.[26] All previously available H_2 blockers, including cimetidine and ranitidine,[27] famotidine[28] and roxatidine[29] have been studied for prophylaxis against Mendelson's syndrome.

The criteria accepted for assessing patients at risk of developing Mendelson's syndrome include a pH < 2.5 and volume of > 25 ml as described by Roberts and Shirley.[4] Although these criteria were based on preliminary unpublished work in the Rhesus monkey they gained widespread recognition and have been applied in most studies, including the present one. Since our work was completed, Raidoo *et al.*[30] have challenged these criteria and have suggested that the critical volume for acid aspiration can be increased to at least 50 ml of pH1 (0.8 ml/kg). This new criteron requires further substantation. James *et al.*,[17] in a study of volume and pH of gastric contents in rats, demonstrated that samples with low volume and low pH resulted in high mortality, whilst large volumes were tolerated at higher pH. Plourde and Hardy[31] demonstrated in cats that the residual gastric volume needed to produce regurgitation under general anaesthesia is at least 20 times greater than the volume required to produce pulmonary damage by intratracheal injection (0.3 ml/kg, assuming a pH of 2.5 or less). The majority of studies, including the present one, have used blind gastric tube aspiration as the method of measuring the volume of gastric contents. This may underestimate the true total gastric volume, as has been shown by Taylor *et al.*[32] who measured true total gastric volume aspirated through a visually guided fibreoptic gastroscope. The blind gastric aspirate volume underestimated true total gastric volume by an average of 14.7 ml and this was statistically significant, hence a critical volume of gastric contents required to cause aspiration pneumonitis in man is difficult to define and measure. We made every effort to empty the stomach completely by using a large bore orogastric tube with multiple side holes, confirmed its position in the stomach by auscultation and asked the surgeons, where possible, to confirm its placement under direct vision. In addition, if no aspirate was obtained, the tube was withdrawn and re-inserted. Furthermore, in patients in the N and the R groups in whom no aspirate could be obtained, all the patients had blood levels of the drugs in excess of the quoted therapeutic ranges, except for two patients in the N group in whom the blood levels were below the therapeutic levels. This could mean that the drugs were effective and no aspirates could be obtained.

In the present study there was no difference overall in the volumes of gastric aspirates between groups. This is in agreement with other studies using the same methodology.[26,29,33–36] When data were analysed for pH alone there were no differences between the nizatidine and ranitidine groups, but both these groups had higher median pH values when compared to placebo. The number of patients in the placebo group with a pH < 2.5 was significantly higher than in the nizatidine and ranitidine groups. Although there were six patients in the ranitidine compared to two in the nizatidine groups with pH < 2.5, this did not achieve statistical significance.

One of the disadvantages of oral ranitidine in clinical practice is its inability to raise the gastric pH before a latent period of between 45 minutes[37] and 2 hours.[38] This has been confirmed in the present study where six out of 21 patients (28.6%) in the ranitidine group had pH < 2.5 when the

interval between drug administration and induction of anaesthesia was between 45 and 90 minutes (three of these patients also had volumes > 25 ml). In the nizatidine group, during the same time interval, only two out of 15 patients (13.3%) had pH < 2.5 and neither had volume > 25 ml. In one of these a second sample taken before extubation at 96 minutes showed a pH 2.6. Although these numbers did not reach statistical significance, in clinical practice nizatidine seems to have a shorter latent period compared to ranitidine and may be more appropriate to use, especially when a quicker onset of action is desired. There were no major side effects attributable to the drugs in either of the treated groups.

Thus nizatidine appears to be a suitable H_2 antagonist to use for prophylaxis of acid aspiration pneumonitis and investigation of its value should be extended for prophylaxis in patients in the high risk groups mentioned before.

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Timing of surgery in congenital diaphragmatic hernia

Low mortality after pre-operative stabilisation

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Summary

Eighty-six consecutive patients with congenital diaphragmatic hernia presenting within 6 hours of birth to a regional neonatal surgical unit were reviewed. Patients were managed under a policy of delayed surgery which has evolved during the 6-year study period. Overall survival (to leave hospital) was 70.9%. There were only seven postoperative deaths (10.3% of operations). Analysis of the 25 deaths in the light of postmortem findings and published exclusion criteria indicates that the availability of extracorporeal membrane oxygenation would have made little difference to overall survival.

Key words

Hernia; diaphragmatic, congenital.

Mortality from congenital diaphragmatic hernia (CDH) has been largely unaffected by the enormous advances made in neonatal intensive care, and remains approximately 50%.[1] Typically, death results postoperatively from the high pulmonary vascular resistance associated with pulmonary hypoplasia, which promotes right-to-left shunting, reversion to the transitional pattern of circulation and fatal hypoxia.

Recently two contrasting strategies have emerged which offer some hope of improving survival. Extracorporeal membrane oxygenation (ECMO) has been used after emergency surgery in at least 19 centres in the USA.[2] In 30 consecutive cases of CDH at one centre,[1] 44% of patients received ECMO and a further 20% were considered but excluded by specific criteria. Reported survival was 75%. This treatment is complex and expensive and has yet to find favour in European centres.

An alternative strategy has been to abandon the tradition of emergency surgery in order to optimise the pre-operative condition of the baby. However, early reports of small series[3–5] have shown no improvement in survival above the world average. Our Regional Neonatal Surgical Unit, which serves a population of over four million, abandoned emergency surgery in 1983 and criteria for delaying surgery have been developed. This report summarises our experience over the subsequent 6 years.

Methods

Eighty-six consecutive patients with congenital diaphragmatic hernia presented with respiratory distress within 6 hours of birth or after antenatal ultrasound diagnosis. Fourteen of the 15 babies with antenatal diagnosis were delivered in our hospital. Babies born in other hospitals were usually collected by road by our 'flying squad'. Since 1983 only one death is known to have occurred before the patient reached our hospital. Over 75% of our catchment population lies within one hour of road transportation.

In most cases the trachea was intubated with a nasotracheal tube and ventilation was controlled with the aid of a muscle relaxant during transfer. One child was brought in good condition without a tracheal tube. On arrival in our unit medical treatment was instituted, aimed at stabilising the condition of the baby before surgery. No emergency surgery was carried out. Conventional positive pressure ventilation was used, facilitated by infusion of tubocurarine, atracurium or pancuronium. Tolazoline and dopamine were employed to manipulate the pulmonary and systemic circulations if indicated. The stomach was kept decompressed by a nasogastric tube, passed before transport to our unit.

Patients were admitted under the care of five consultant paediatric surgeons. Early in the study period opinions differed amongst the surgeons and paediatric anaesthetists as to the optimum timing of surgery. As experience of prolonged nonoperative management grew, agreed criteria for optimum timing of surgery evolved. These were a period of at least 24 hours of stable or improving gas exchange, and an inspired oxygen fraction requirement of not more than 0.5 to maintain an arterial oxygen tension of 8 kPa. When these criteria were met, surgery was planned for a convenient time, as an elective procedure. Babies who

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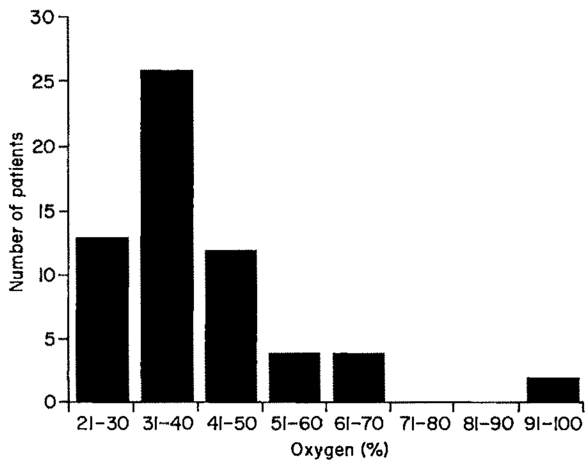

Fig. 1. Inspired oxygen requirement (%) at surgery (n = 68).

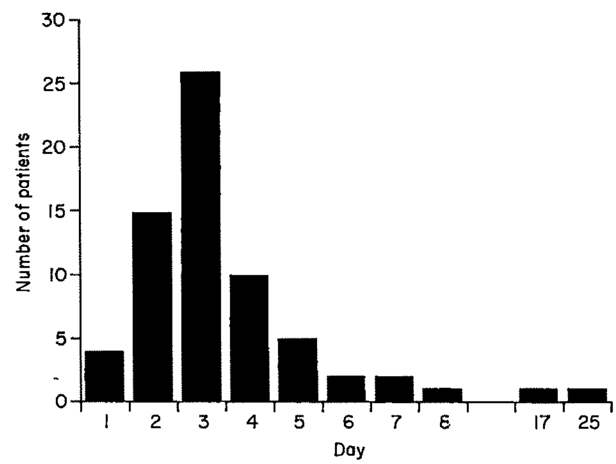

Fig. 2. Timing of operation, by calendar day of life.

deteriorated despite maximal medical treatment were not offered surgery. This left a small group of babies who survived without meeting the criteria for surgery; these babies were ultimately operated upon at some time after 7 days, the latest time at which we had noted improvement in gas exchange.

Results

The mean gestational age of the 86 babies was 40 weeks (range 32 to 42). There were 12 premature babies born at 36 weeks or less. Birth weights ranged from 1.0 to 4.7 kg (median 3.1). Ten babies weighed less than 2 kg.

Fifty-seven of the 68 (84%) babies who received surgery met the criterion for $Pa\text{O}_2/F\text{IO}_2$ at the time of surgery. As reduction in oxygen requirement was noted in some patients as late as day 6, the application of this criterion became progressively stricter, so that of the last 57 cases only four were accepted for surgery at an $F\text{IO}_2$ requirement above 0.5. Three of these had been delayed to day 6 or beyond; the fourth was operated on at day 4 with an $F\text{IO}_2$ of 0.7. Figure 1 shows the oxygen requirements of patients at the time of surgery.

No child underwent immediate surgery. Figure 2 shows the timing of the 68 operations by calendar day of life. Fifty-four percent of operations occurred on days 3 or 4. The longest elective delay was 17 days. A further child was operated on at day 25 due to delay in diagnosis at the referring hospital, despite the need for controlled ventilation from birth. In the first 4 years, five babies, all under the care of the same surgeon, underwent operation between 6 and 11 hours after birth. Another two had been allowed to stabilise overnight but were operated on at 19 and 20 hours from birth. No surgery was carried out within 24 hours in the last 48 consecutive cases.

No surgical complications occurred which were attributable to delay in reduction of the hernia. Two babies who died on day 5 without operation were noted at autopsy to have developed a gastric ulcer, a possible complication of

Table 1. Details of babies who died in the postoperative period.

Patient	Surgery (day)	Death (day)	Pathology
1	2	3	Aortic coarctation Hypoplastic left atrium Lung weight 38% of predicted
2	2	24	32 week gestation Pneumonia Periventricular leucomalacia
3	3	43	Patent ductus arteriosus Repeated pulmonary infection Respiratory failure
4	4	48	Pneumonia
5	17	228	Intrauterine cytomegalovirus Prune belly Cerebral atrophy
6	8	13	No autopsy $F\text{IO}_2$ 1.0 at surgery Dopamine+tolazoline
7	7	15	No autopsy $F\text{IO}_2$ 0.7 at surgery Dopamine+tolazoline

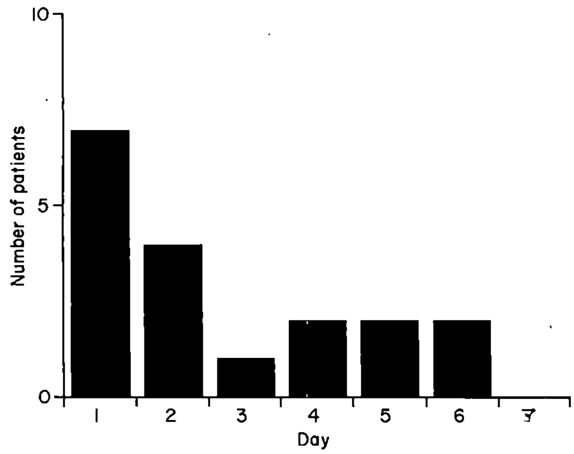

Fig. 3. Time of pre-operative death, by calendar day.

treatment with tolazoline.[6] No anaesthetic complications were reported and no cases of acute deterioration occurred during surgery.

Twenty-five of the 86 babies (29%) died. Sixty-six patients were transferred after birth; 17 died (26%). Nine of the 20 babies born in our hospital died (45%), all but one with antenatal diagnosis. There were seven postoperative deaths (10.3% of operations; Table 1) and 18 pre-operative deaths (Fig. 3, Table 2). Six of the 12 premature babies survived. All three babies who underwent surgery after 7 days despite failing to meet the criteria for oxygenation died (Table 1). The changes in mortality during the study period are shown in Table 3. Because of fluctuations in yearly numbers these data are presented in groups of 14 consecutive patients before and after the change in operating policy.

Discussion

The mortality of 29.1% in 86 consecutive cases of congenital diaphragmatic hernia appears to be the lowest yet reported in a series of this size and is considerably below the world average of 50%. This is also the largest series which has involved delayed surgery. From 1976 (when our regional unit opened) until 1983, with a conventional policy of emergency surgery, there were 58 cases with 27 deaths (47%), 25 of which were postoperative. Our survival rate is now higher despite the fact that 18 of the 25 deaths occurred in babies who received no operation (Table 3).

CDH is a condition in which a significant mortality is inevitable, due not only to the spectrum of severity of pulmonary hypoplasia but also to the frequency of major coexisting anomalies. A successful management policy should ensure that no child who is incapable of ultimate survival should be subjected to surgery (or ECMO).

Table 2. Pre-operative deaths and suitability for ECMO.

Total deaths: 18	
ECMO exclusion criteria[1]	
Gestation < 35 weeks	1
Serious coexisting anomaly	
Heart	3
Chromosome	2
No 'honeymoon'	2
Lung weight < 35% of predicted	6
Possible ECMO candidates	4

Table 3. Mortality before and after change in operating policy, shown as number of deaths in groups of 14 consecutive patients.

Emergency surgery		Delayed surgery	
Years	Deaths	Years	Deaths
1976–78	6	1983–84	5
1979–80	6	1984–85	5
1981–82	7	1985–86	3
1982–83	6	1986–87	4
		1987	4
		1988–89	4

However, the early identification of potential survivors has been the subject of much debate.[7,8] Analysis of the deaths in our series suggests that our two criteria for surgery offer good selection of potential survivors.

Table 1 gives details of the seven postoperative deaths. Patient 1 presented very early in the series and was operated on at 19 hours before full cardiovascular assessment had been made. His lung weight (as a percentage of predicted value for body weight)[9] was close to the limit for viability. If this child had appeared later in the series the likely outcome would have been death without operation. Patients 2, 3 and 4 succumbed late to infection superimposed on hypoplastic lungs; patient 2 was also premature. Patient 5 was very unstable pre-operatively and the subject of our longest elective delay. Our caution was justified since it took 6 months to achieve tracheal extubation and he died of respiratory failure without leaving hospital. Patients 6 and 7 required an F_{IO_2} of 1.0 and 0.7 respectively at 7 days, and dopamine and tolazoline were needed also. They underwent surgery when it was believed that no further pre-operative improvement was likely. Both died after operation without any improvement; pulmonary hypoplasia was the major cause.

The timing of pre-operative deaths is shown in Figure 3. Sixty percent of deaths occurred within 48 hours; the latest was on day 6. We appear to be unique in allowing death to occur without the baby having surgery. Have we by this policy allowed viable babies to die? Should we have offered them ECMO when conventional intensive care was failing? Table 2 details the deaths according to the published criteria for exclusion from ECMO therapy.[1] Eight patients would have been excluded. Postmortem findings showed that a further six patients had lung weights below 35% of predicted,[10] which we believe to be incompatible with survival. There remained only four nonsurvivors in whom ECMO might have been of benefit. These are detailed in Table 4. Two babies died early and did not have post-

Table 4. Possible candidates for ECMO.

Day of death	Pathology
6	Severe IRDS Early pneumonia Lung weight 63% of predicted
6	IRDS of hypoplastic lung Early pneumonia Lung weight 46% of predicted
2	No autopsy
3	No autopsy

IRDS, infant respiratory distress syndrome.

mortem examination; consequently we do not know if the lung size was compatible with prolonged life. The two remaining cases had infant respiratory distress syndrome with early pneumonia and died on day 6.

It seems likely that ECMO would not have had a major impact on overall mortality in our unit because survival of CDH patients given ECMO in a multicentre study was only 58%.[2] ECMO has been used in up to 40% of cases in some reports from the USA. We can only conclude that many patients undergo this treatment who would not be considered to require it in our unit. It may be argued that our patients are selected and are not as ill as those in the US centres. However, we do not believe that our population differs significantly from that of any large neonatal surgical unit, nor that we miss any more patients who die before referral than do other large units. We also receive antenatal transfers, who have a mortality of up to 80%.[11]

There is good reason to believe that our low mortality is related to the timing of surgery. Surgical reduction of the hernia does not improve lung mechanics, and may make them worse.[12] Our policy has therefore been to continue meticulous medical management and to delay surgery until no further improvement in lung function occurs. There is some physiological data to support our finding that oxygen requirements do fall during the first days of life. It is known that pulmonary vascular resistance (PVR) decreases during the first week[13] and that by day 3 the ratio of wall thickness to lumen size of small pulmonary arteries has fallen.[14] It could be that this normal reduction in PVR occurs also in the CDH patient provided that the trigger factors for pulmonary vasoconstriction can be avoided by meticulous intensive care. A recent study of pre-operative pulmonary arterial pressure monitored by echocardiography lends support to this view, but included only eight patients.[15] We find that improvement in gas exchange occurs over a period of several days and this may account for our greater success compared with centres which opt for shorter delay.[2-4]

Unfortunately, meaningful statistical comparison with our earlier results is not possible because of other alterations in overall management since 1983, which include the major involvement of specialist paediatric anaesthetists in the intensive care of these patients.

In summary, our view is that the management of CDH is essentially that of pulmonary hypoplasia and transitional circulation. We believe that the concept of delaying surgery until optimal gas exchange and pulmonary haemodynamic stability have been achieved is theoretically sound. In our hands this has resulted in a survival rate which represents a considerable improvement over conventional management.

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A comparison of different pre-oxygenation techniques in the elderly

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Summary

The efficacy of five different techniques of pre-oxygenation before a modified rapid intubation sequence was assessed, using oxygen saturation measurement, in patients aged over 65 years. Twenty patients in each group were pre-oxygenated using four deep breaths or normal tidal breathing for 1, 2, 3, or 4 minutes. The acceptable period of apnoea was defined as the time taken to desaturate to 93%. The mean times (SD) taken to reach this end-point were 3.7 (1.6), 4.1 (1.2), 5.4 (1.7), 5.4 (1.4) and 5.2 (1.7) minutes respectively. The apnoea times with 2, 3 and 4 minutes pre-oxygenation were not significantly different from each other but were significantly longer than after four deep breaths and 1 minute. It is concluded that a pre-oxygenation period of at least 2 minutes should be employed in the elderly before a rapid sequence induction.

Key words

Anaesthesia; pre-oxygenation.
Induction; rapid sequence.

Pre-oxygenation is commonly employed in anaesthesia particularly before induction in emergency situations requiring a rapid intubation sequence. There have been many studies of different methods of pre-oxygenation ranging from four deep breaths, to several minutes of breathing oxygen.[1-3] These have been carried out in the young and healthy. There are increasing numbers of elderly patients.[4] Ageing has several effects on lung function which may influence oxygenation and therefore have implications for pre-oxygenation technique used in the elderly.[5] The time for which pre-oxygenation should be carried out and the safe period during which elderly patients can be left apnoeic are not well documented. In the present study this has been examined by measurement of oxygen saturation during a modified rapid intubation sequence.

Methods

One hundred ASA grade 1 or 2 patients aged over 65 years were included in the study for which informed consent and Ethics Committee approval had been obtained. Patients with ischaemic heart disease, obstructive airways disease, weight greater than 120% of ideal, anaemia, or smoking within 3 months of surgery were not studied. Premedication was with 5–10 mg of diazepam given 90 minutes before operation. All patients were monitored with ECG, noninvasive arterial pressure and pulse oximetry via a finger probe from the time of their arrival in the anaesthetic room until extubation of the trachea. The pulse oximeter used was a Nellcor N100, which averaged over 3 seconds with a stated accuracy of (SD) 2%.

Pre-oxygenation was carried out with 100% oxygen, after a resting period of 5 minutes, using a nonrebreathing system at a fresh gas flow of 10 litres/minute. The reservoir bag was observed at all times so that the oxygen flush button could be pushed to refill the bag instantly if it appeared to collapse.

Twenty patients in each group were allocated to one of five pre-oxygenation methods. These were four deep breaths taken slowly over a period of 30 seconds, or normal breathing for 1, 2, 3, or 4 minutes. The facemask was applied firmly on the face but not so tightly as to cause any discomfort. The anaesthetic sequence, which started 30 seconds before the end of pre-oxygenation, consisted of administering vecuronium 0.1 mg/kg and fentanyl 1 μg/kg, followed 30 seconds later by thiopentone 3–5 mg/kg. Intubation of the trachea was carried out 90 seconds after the administration of vecuronium. The start of pre-oxygenation and administration of vecuronium occurred simultaneously in those who received four deep breaths.

Ventilation was not assisted before tracheal intubation and the tracheal tube was left open to the atmosphere until the oxygen saturation reached the study end-point of 93%. If the study end-point had not been reached in 3 minutes patients were given increments of thiopentone 0.5–1 mg/kg every 2–3 minutes. The first five patients in each group also

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had a 24 gauge cannula inserted into the radial artery of the nondominant hand for collection of arterial blood samples.

The resting peripheral oxygen saturation (Spo_2), Spo_2 after pre-oxygenation, and at intubation, and the time to a reduction of each one percent in Spo_2 up to 93% were recorded. Arterial blood samples were withdrawn at rest, after pre-oxygenation and at 93% Spo_2. These were stored in ice and analysed within 15 minutes. Results were analysed using analysis of variance, Duncan's test for multiple comparisons, and the Kruskal–Wallis test.

Results

The groups did not differ with respect to age, weight, or sex distribution (Table 1). There was no difference among the groups in terms of their average resting Spo_2, or the Spo_2 after pre-oxygenation and at intubation (Table 2). No patient had an Spo_2 of less than 97% at intubation.

Figure 1 shows the rate of decline in Spo_2 in the five groups in terms of the mean times taken to each percentage point decrease in saturation up to 93%. It shows that the decline in Spo_2 is slower at first, decreasing only 2–3% in the first 2 to 3 minutes. Thereafter, desaturation occurs more rapidly. It also shows that a saturation of 93% is reached earlier in those pre-oxygenated with four deep breaths or for 1 minute. The mean times to reach an Spo_2 of 93% in the five groups are given in Table 3, and show that the times of 3.7 (1.6 SD) minute and 4.1 (1.2) minute in the four deep breath and 1 minute groups respectively were not significantly different from each other. These times, however, were significantly shorter than the times of 5.4 (1.7), 5.4 (1.4) and 5.2 (1.7) minutes respectively in the 2, 3, and 4 minute pre-oxygenation groups. There was no significant difference in these times in the 2, 3, and 4 minute groups.

The arterial oxygen and carbon dioxide tensions when measured (Pao_2, $Paco_2$) are given in Table 4. There was no difference among the groups at rest, or at the study end-point of 93% Spo_2 either in the Pao_2 or the $Paco_2$. There was also no significant difference between the resting Pao_2 breathing room air and the Pao_2 at the study end-point of 93% Spo_2 within each group. There was no significant difference between the groups in Pao_2 at peak oxygenation.

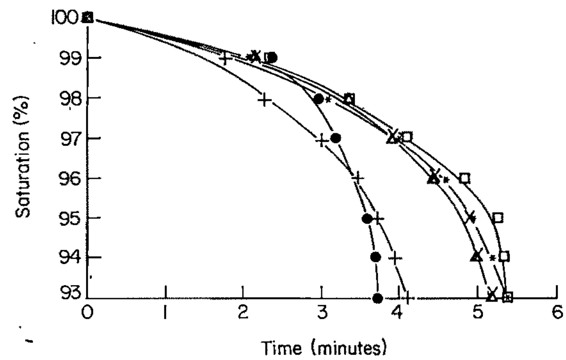

Fig. 1. Mean times to each per cent decrease in oxygen saturation during apnoea after different methods of pre-oxygenation. ●, four breaths; +, 1 minute; * 2 minutes; □, 3 minutes; △, 4 minutes.

Discussion

Pre-oxygenation techniques can be studied by assessing denitrogenation, blood gas analysis, or Spo_2. In this study we have used the noninvasive Spo_2 measurement with blood gas analysis in a representative sample. In carrying out a study in apnoeic patients we were anxious to avoid exposing patients to an unacceptable risk of continuing desaturation after the study end-point. To achieve this the tracheas of all patients were intubated under a modified rapid intubation sequence so that a tracheal tube was in place before the study end-point to allow instantaneous and efficient ventilation with 100% oxygen.

There are several changes that occur during the process of ageing that may influence the period of pre-oxygenation that should be used in the elderly, and the subsequent time to desaturate to a given level. On the one hand, the basal oxygen consumption declines with age (from about 143 ml/minute/square metre in a male aged 20 years to 124 ml/minute/square metre in a male aged 60 years)[5] so

Table 1. Patient characteristics, mean (SD).

	Four breaths group	1 minute group	2 minutes group	3 minutes group	4 minutes group
Age; years	78 (6)	77 (8)	77 (6)	77 (7)	77 (5)
Weight; kg	60 (11)	63 (13)	62 (11)	56 (10)	65 (14)
Sex; M/F	7/13	8/12	8/12	8/12	7/13

Table 2. Oxygen saturation data Spo_2 % median (range).

	Four breaths group	1 minute group	2 minutes group	3 minutes group	4 minutes group
At rest	97 (94–100)	97 (94–98)	96 (94–99)	97 (95–99)	96 (94–99)
After pre-oxygenation	100 (98–100)	99 (99–100)	99 (99–100)	100 (98–100)	99 (98–100)
At intubation	99 (97–100)	99 (99–100)	99 (99–100)	100 (99–100)	99 (97–100)

Table 3. Mean time to 93% saturation.

	Four breaths group	1 minute group	2 minutes group	3 minutes group	4 minutes group
Mean	3.7	4.1	5.4*	5.4*	5.2*
SD	1.6	1.2	1.7	1.4	1.7
Range	1.9–8.0	2.6–6.7	3.0–8.1	2.7–7.3	2.8–8.6

*$p < 0.05$ in comparison to four breaths and 1 minute group.

Table 4. Pa_{O_2} and Pa_{CO_2} kPa (SD).

	Four breaths group	1 minute group	2 minutes group	3 minutes group	4 minutes group
Pa_{O_2}					
Resting	11.0 (1.5)	10.7 (0.9)	11.5 (1.1)	11.6 (1.6)	10.7 (1.2)
Peak	32.5 (6.4)	37.5 (4.4)	44.7 (12.0)	42.3 (7.5)	45.9 (17.1)
At 93% Sp_{O_2}	10.3 (0.9)	10.4 (0.5)	11.2 (0.8)	11.3 (1.7)	11.1 (0.9)
Pa_{CO_2}					
Resting	5.2 (0.6)	5.6 (0.4)	5.6 (0.4)	5.5 (0.4)	5.2 (0.4)
At 93% Sp_{O_2}	7.6 (0.5)	8.0 (0.5)	9.1 (1.0)	8.0 (0.8)	8.0 (1.0)

that the demand for oxygen is less, while on the other hand changes in lung function make oxygen uptake less efficient. In particular the closing volume increases with age leading to less efficient denitrogenation during a pre-oxygenation sequence at normal tidal volumes; this could mean that longer periods of pre-oxygenation could be required in the elderly.

It appears that larger, slower breaths which create prolonged and greater subatmospheric intrapleural pressure because of more even distribution of inspired gases[6] are relatively unimportant since the four-breath technique in the present study did not result in longer apnoea times. Similar results have been shown in the young with the four deep-breath technique. This does not result in so long a period to desaturate to 93% Sp_{O_2} (6.3 minutes) as 3 minutes of pre-oxygenation at normal tidal volumes (8.6 minutes).[7] It also appears that any reduction in oxygen demand in the elderly does not compensate fully for less efficient oxygen uptake since the mean times to 93% saturation in our elderly patients are approximately half those reported for equivalent pre-oxygenation periods in the young.[7] A further difficulty with the deep-breath technique lies in how far each breath is actually a vital capacity breath and not just a 'deep' breath. In one of the few studies looking at pre-oxygenation in the elderly, the 12 patients in a 'vital capacity breath' group were rehearsed in the technique, but still only sustained a period of 3.2 minutes apnoea before 93% saturation was reached.[8] In our study, patients were not rehearsed, but were simply encouraged to take deep breaths, since this was considered to be more representative of what happens in actual clinical practice. It is possible that in the supine position the elderly patient cannot take true vital capacity breaths.

There are several compensatory mechanisms available to patients when arterial oxygenation decreases. These include alterations in cardiac output to distribute oxygenated blood to major organs and a shift in the oxygen dissociation curve to the right to maintain the venous P_{O_2}. The lowest tolerable Pa_{O_2} in humans is of the order of 4 kPa assuming maximum cerebral vasodilation,[9] a compensatory mechanism which might be uncertain in the elderly. We therefore adopted a study end-point of 93% Sp_{O_2} which would result in a minimal change in Pa_{O_2}, although this is only a small component of total oxygen content.

Our baseline measurements of Pa_{O_2} were made under clinical conditions with premedicated patients in the supine position but they yielded values similar to those found in work relating Pa_{O_2} to age.[4] The actual peak Pa_{O_2} was not statistically different between the groups, although groups given longer periods of pre-oxygenation had higher Pa_{O_2} values. This may be due to the relatively small number of patients within each group ($n = 5$) in whom arterial blood gas analysis was carried out. It was satisfying to note that the Pa_{O_2} whilst breathing room air at the start of the study, thus confirming the safety of using 93% Sp_{O_2} as the safe end-point in the study.

We did not find any difference in the apnoea time between the 2, 3, and 4 minute pre-oxygenation groups in the present study. However, not only was the rate of desaturation slower in these groups (Fig. 1), but also an average of more than an extra minute of apnoea time was gained. The clinical significance of the extra period of apnoea gained by longer periods of pre-oxygenation is open to debate since our results could be interpreted to suggest that the four deep-breath technique is an acceptable method of pre-oxygenation since the patients in the four-breath group were intubated with time to spare. If, however, we consider the range of results (Table 3) we can see that the only group with a lower range for desaturation time under 2 minutes was the four-breath group, so that the margin of safety was limited. Since difficulties with intubation occur unexpectedly we believe it is prudent to use pre-oxygenation periods of 2 minutes or more.

In conclusion, the results from the present study show that although four deep breaths and 1 minute of pre-oxygenation give average apnoea times of 3.7 (1.6) and 4.1 (1.2) minutes, a minimum of 2 minutes pre-oxygenation gives significantly longer time to desaturate to 93%. Pre-oxygenation for up to 4 minutes does not appear to confer any significant advantage.

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A comparison of azapropazone and aspirin for pain relief following dental extractions

M. A. GARRIOCH, G. J. WARDALL AND W. FITCH

Summary

Eighty patients received one of three treatments after elective dental surgery involving multiple extractions. Group A received aspirin 600 mg, group B azapropazone 300 mg and group C azapropazone 600 mg. All drugs were administered in a double-blind fashion. Quality of analgesia was unsatisfactory for all treatments; over 30% of patients required supplementary analgesia with an opioid. In addition there were a large number of withdrawals from the study. There were no significant differences in analgesic efficacy between groups.

Key words

Analgesics; aspirin, azapropazone.
Surgery; dental.

The pain associated with multiple extractions and other surgical procedures in the mouth provides a useful model with which to study the analgesic properties of peripherally acting analgesics and anti-inflammatory drugs. There are several reasons for this. The intensity of the pain is sufficient to permit a meaningful assessment of analgesia *per se*, there is considerable associated soft tissue swelling and trismus, and it is easy to obtain a large number of otherwise healthy individuals who are willing to take part in such a study.[1]

Prostaglandins (notably PGE_2, $PGF_{2\alpha}$, and prostacyclin) appear to have a role in mediating pain by sensitising peripheral pain receptors to mechanical and chemical stimulation.[2–6] In addition, a central component has been described. Nonsteroidal anti-inflammatory drugs (NSAIDs) are believed to act mainly by inhibiting the enzyme cyclo-oxygenase and thus prevent the synthesis of prostaglandin.

Azapropazone is a pyrazole-derived NSAID used widely in the treatment of rheumatic conditions. It has analgesic, anti-inflammatory, antipyretic and uricosuric properties;[2,7] however, few data exist as to the efficacy of this drug for postoperative analgesia. The objectives of this study were to evaluate this aspect of its pharmacological profile; to determine, to a limited extent, the dose-response relationship of the drug, and to compare the actions of azapropazone with those of a standard analgesic, namely aspirin.

Methods

Eighty-six patients, male or female, aged 18 to 50 years, who were ASA grade 1 or 2 and scheduled to undergo elective oral surgery involving multiple extractions were entered into the study. No patient was included who had known hypersensitivity to NSAIDs, had a history of peptic ulceration or gastrointestinal bleeding, had received medication with NSAIDs or opioids in the 24 hours before operation, had any bleeding disorder or who required anticoagulant therapy. Patients were also not studied if they were unable to follow the design of the study or give informed patient consent. Ethics committee approval and informed patient consent were obtained.

A standard anaesthetic technique was employed. Premedication was with temazepam 20 mg (patient weight < 50 kg) or 30 mg (patient weight > 50 kg), given by mouth 1.5 to 2 hours before operation. Anaesthesia was

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induced with thiopentone 5 mg/kg and neuromuscular blockade obtained with vecuronium 0.1 mg/kg. Nasotracheal intubation was performed and a throat pack inserted. Anaesthesia was maintained with nitrous oxide and enflurane in oxygen, supplemented by fentanyl 1 μg/kg every 30 minutes. The patients' lungs were ventilated mechanically. Residual neuromuscular blockade was antagonised with neostigmine 2.5 mg plus glycopyrronium 0.5 mg. Electrocardiogram and arterial pressure were monitored noninvasively throughout the procedure.

At the conclusion of surgery patients were transferred to the recovery room where they were questioned at 15 minute intervals about their pain. Treatment of any pain was provided in one of three groups A, B or C as outlined below.

The study drug was administered by mouth on a double-blind and randomised basis when the patient first complained of pain in the postoperative period, provided that this occurred within the first 4 postoperative hours.

Group A received aspirin 600 mg, group B azapropazone 300 mg, and group C azapropazone 600 mg. Morphine 10 mg was given intramuscularly as a rescue analgesic if adequate pain relief was not obtained within 90 minutes of administration of the drug. If supplementary analgesia was required because of the return of pain after initially adequate analgesia, paracetamol 1 g was given by mouth.

Pain was assessed using a 10 cm visual analogue scale (VAS) and by a four-point ordered-category scale as follows; 0, no pain; 1, mild pain; 2, moderate pain; 3, severe pain. The degree of postoperative trismus was assessed by determining the extent of mouth opening (measured as the distance between upper and lower incisors on full opening of the mouth, using metal calipers) and noting any changes in measurements postoperatively. Assessments were carried out at the time of first request for analgesia time 0, and at 0.5, 1, 2, 4, 6 and 8 hours thereafter, and finally on the morning of the following day. Mouth opening was assessed before operation in addition to the above times. Patients who were withdrawn from the study were recorded as such, together with the reason for their withdrawal. The need for additional analgesia was noted, as was any evidence of postoperative haemorrhage and the occurrence of any other side effects.

Venous blood samples (10 ml) were taken for azapropazone assay from 17 patients in group B and 20 in group C at 30 minutes and at 1, 2, 4, 6 and 8 hours. Azapropazone concentrations were analysed using a modification of that method described by Farrier.[24] This analysis was used to avoid interference by paracetamol. The method is linear to above 100 μg/ml. The coefficient of variance was at 10 μg/ml 4.9%, and at 50 μg/ml 3.8%. Recoveries were better than 95%.

Statistical significance for any differences between treatments was taken as $p < 0.05$. Data were assessed for suitability for parametric analysis of variance (ANOVAR). Sex, use of rescue and supplementary analgesia, numbers of withdrawals and incidence of side effects were assessed by Chi-squared tests. Mouth opening and VAS pain scores were assessed by one-way analysis of variance at each time of measurement, and further compared by covariant analysis; the covariate was the pre-induction and baseline (T = 0) values for mouth opening, and the baseline values for VAS. Category pain scores were assessed initially by Chi-squared tests at each time point, and subsequently changes from the baseline value were analysed in a similar manner. Where treatment differences were indicated by the analysis of variance and covariance, these were tested further using Duncan's multiple range test.

Table 1. General patient description, mean (SD).

	Ages; years	
Group A (n = 29)	24.4	(5.7)
Group B (n = 24)	23.2	(5.4)
Group C (n = 28)	26.0	(7.1)
	Weight; kg	
Group A (n = 29)	63.9	(10.1)
Group B (n = 25)	59.6	(10.1)
Group C (n = 26)	65.1	(11.4)
	Males	**Females**
Group A	8	20
Group B	5	19
Group C	6	22

Results

Six patients did not require analgesia during the first 4 hours after operation and therefore did not contribute to the results of the study. Of the remaining 80 patients, 28 received aspirin 600 mg (group A), 24 azapropazone 300 mg (group B) and 28 azapropazone 600 mg (group C). There were no significant differences between the groups with regard to age, sex and weight distribution (Table 1), initial baseline pain score, and extent of surgery. The mean time of study drug administration was 30.5 minutes after awakening. Thirty-seven percent of patients who requested analgesia did so immediately on awakening; 70% of patients had received study medication within the first postoperative hour and 97% within 90 minutes.

Analysis of variance for pain scores (Fig. 1) indicated significant treatment differences at one hour after administration only; group B had a significantly lower mean score than group C. Group A was intermediate between the other groups and did not differ significantly from either. Analysis of covariance indicated significant effects of the initial (T = 0) value at 0.5, 1, 2 and 8 hours only and significant treatment differences at one hour only; group B had a significantly lower mean score than groups A or C.

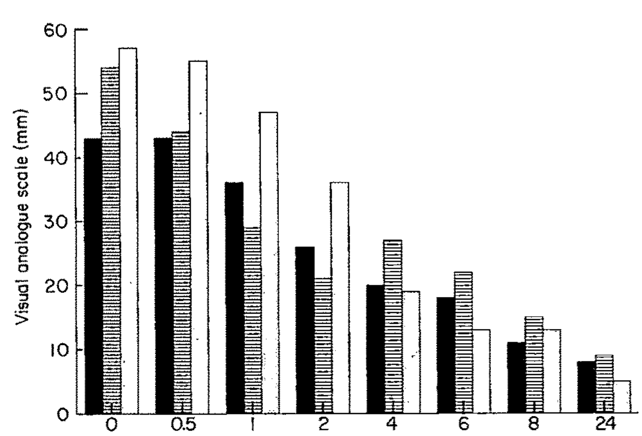

Fig. 1. Visual analogue scale (mm) after the operation (■, aspirin; ▤, azapropazone 300 mg; □, azapropazone 600 mg).

Table 2. Pain score frequencies.

Time		Score				Chi-squared	d.f.	p
		0	1	2	3			
0 hours	Group A	0	11	12	5	4.826	4	ns
	Group B	1	5	8	9			
	Group C	0	5	13	9			
0.5 hours	Group A	0	10	12	6	1.347	4	ns
	Group B	1	7	11	5			
	Group C	1	5	14	7			
1 hour	Group A	2	12	9	3	6.963	6	ns
	Group B	3	9	8	0			
	Group C	0	10	13	3			
2 hours	Group A	3	16	5	1	2.280	4	ns
	Group B	4	12	2	1			
	Group C	2	13	6	1			
4 hours	Group A	8	11	5	0	9.685	4	< 0.05
	Group B	7	5	5	1			
	Group C	3	16	2	0			
6 hours	Group A	11	7	4	0	6.387	4	ns
	Group B	7	7	3	0			
	Group C	8	13	0	0			
8 hours	Group A	8	13	0	0	0.766	2	ns
	Group B	7	6	1	0			
	Group C	6	9	2	0			
24 hours	Group A	14	7	0	0	3.296	2	ns
	Group B	10	7	0	0			
	Group C	17	3	0	0			

Table 3. Use of rescue analgesia (intramuscular morphine).

Group	Number of patients needing rescue	Time of rescue; minutes, mean (SD) range	*n*
A	9	59 (41) 20–150	8
B	10	53 (33) 15–125	10
C	11	74 (40) 32–180	11

Assessment of the ordered category pain scores (Table 2) at each time point indicated significant differences at 4 hours only; these differences were largely because of the increased frequency of patients scoring one in group C compared to other groups. Analysis of change from the zero time score showed no significant differences between the three groups at any time.

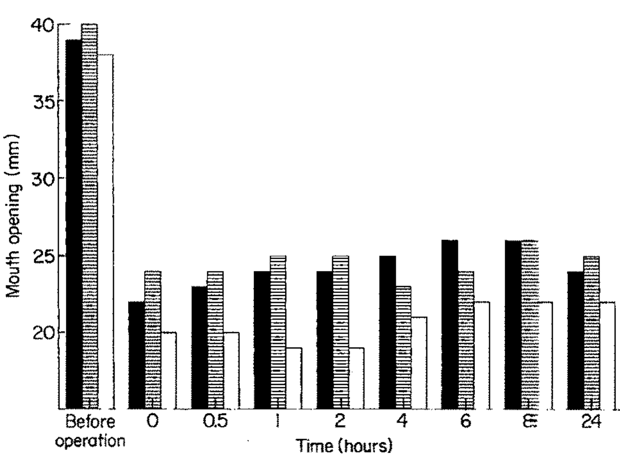

Fig. 2. Mouth opening (mm) before and after the operation (■, aspirin; ▤, azapropazone 300 mg; □, azapropazone 600 mg).

ANOVAR for mouth opening data (Fig. 2) indicated significant treatment differences at one and two hours after drug administration; group C had significantly lower mean mouth opening than A or B. Analysis for covariance indicated significant effects of the T0 value at all times following drug administration, but no effect on the pre-induction value. Analysis of covariance was thus repeated using only the baseline T0 value as covariate and this analysis indicated significant differences at T1 only; again group C had a significantly lower mean mouth opening than A or B.

Supplementary analgesia with paracetamol 1 g was provided for 18 patients (64%) in group A, 14 (58%) in group B and 15 (53%) in group C. There were no significant differences between groups.

Rescue analgesia was needed for 30 patients (Table 3). There were no significant differences between groups either in numbers of patients requiring such analgesia or in the times at which it was administered.

Nineteen patients were withdrawn from the study (Table 4). Of these, 13 withdrawals had inadequate pain relief, even after intramuscular morphine, and six had difficulties with blood sampling or were uncooperative. No significant differences were found between the number withdrawn in each group.

Table 5 gives side effects as volunteered by patients.

Table 4. Patients withdrawn from the study.

Group	Number withdrawn	Remaining	Chi-squared	d.f.	p
A	5	23	0.95	2	ns
B	7	17			
C	7	21			
	Withdrawn for 'inadequate pain relief' (*n*)				
A			3		
B			5		
C			5		

There were no significant differences between groups. Mean plasma azapropazone levels are shown in Fig. 3.

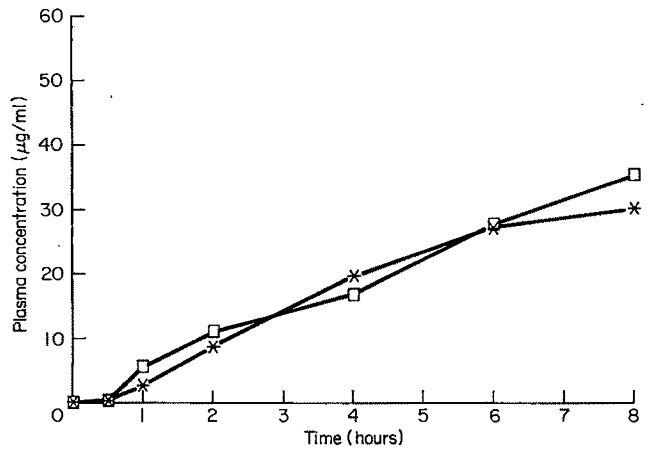

Fig. 3. Plasma azapropazone concentrations (μg/ml) after administration of azapropazone 300 mg and azapropazone 600 mg (□, azapropazone 300 mg; *, azapropazone 600 mg).

Discussion

Several previous studies[1,3,6] attest to the efficacy of orally administered nonsteroidal anti-inflammatory drugs in relieving the pain associated with oral surgery. It is therefore surprising that the main finding of the present study was the disappointing quality of analgesia obtained in all treatment groups. Approximately one third of the patients required the administration of a rescue opioid and a further number were withdrawn when analgesia was considered inadequate, despite the administration of 10 mg morphine. Theoretically, this situation must have arisen because the pain associated with oral surgery was much more severe than anticipated thus it should have been treated with potent analgesics *ab initio*; the drugs employed in the investigation did not possess adequate analgesic properties; the time of drug administration was inappropriate or a combination of all of these.

There is no doubt that the pain experienced by the patient, as indicated by the high initial visual analogue scores, was severe before they requested an analgesic. The day-to-day practice of anaesthesia demonstrates clearly that the control of pain is much easier if an analgesic is administered before the pain becomes severe.[21] Pain is a subjective phenomenon; nevertheless, the relatively unsatisfactory nature of the analgesia obtained in this study may have been due, in part at least, to the stoical nature of the patients; the request for analgesia only occurred once the pain had already become intense. In this context, it may be relevant to note that most of the previous studies on the analgesic efficacy of NSAIDs were carried out in North America and it is conceivable that earlier requests for pain relief yielded more satisfactory results.

Another factor which may be considered is that previous studies were carried out by nonanaesthetists, notably clinical pharmacologists and oral surgeons. It may be that these investigators have a different perception as to what constitutes satisfactory postoperative analgesia. They may also be less willing to administer potent opioid analgesics because of concern about side effects.

The drugs used in the study do undoubtedly possess analgesic properties. Aspirin has been used extensively in the treatment of mild to moderate pain.[5,8–10,14] Azapropazone has been used for some time for the treatment of rheumatic conditions and a large number of studies attest to its analgesic efficacy for this purpose.[18–20] However, certain questions remain unanswered.

We are at a loss to explain why no difference in plasma levels of azapropazone 300 mg and 600 mg doses was shown. In fact all previous work investigating azapropazone has assessed the drug by analgesic activity i.e., ability to modify pain threshold, not by measurement of plasma levels.[23] Thus we believe our work to be the first to compare plasma level with analgesic effect. Work previously done in healthy human volunteers[15] indicates that peak plasma levels of azapropazone occur about 90 minutes after administration, thus we were disappointed to find that this did not occur in our study. The timing and method of drug administration was also shown to be inappropriate because postoperative plasma drug concentrations were so low they gave minimal analgesia. It should also be noted that a high degree of variability exists in these postoperative plasma concentrations; some patients had only traces of azapropazone in the blood up to 4 hours after administration, whereas in a small minority concentrations were surprisingly high. There are several possible explanations for this. Gastric emptying may well have been markedly reduced because of the pain experienced by some patients. Another theory is that the administration of opioids during the operation inhibited the entry of drug into the duodenum thus slowing absorption, although recent work[22] suggests that fentanyl may not have this effect.

In retrospect, it would have been useful to measure the postoperative concentrations of aspirin to reinforce these findings, but unfortunately this was not done. Previous studies of a similar nature did not include measurement of

Table 5. Side effects.

Group	None	Nausea	Headache	Sore throat	Bleeding	Other
A	18	4	1	2	2	1
B	19	3	1	1	0	0
C	18	3	2	0	2	1

plasma drug concentrations and thus cannot aid our conclusions.

In conclusion, this study, in contrast to previous work, shows that NSAIDs given orally are not an efficacious means of providing analgesia in a large number of patients following dental extractions. We believe that the subject warrants further study by anaesthetists, since they are often involved in the initial prescription of postoperative analgesia for such patients. Our findings do highlight the importance of achieving, and verifying, therapeutic concentrations of such drugs (particularly after oral administration) before drawing conclusions on analgesic efficacy.

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Comparison of high and low doses of suxamethonium

K. G. STEWART, P. M. HOPKINS AND S. G. DEAN

Summary

In a double-blind study, 67 young adult patients undergoing anaesthesia for dental extractions were allocated at random to receive either 0.5 mg/kg or 1.5 mg/kg suxamethonium. A greater increase in arterial pressure was seen following induction in the 1.5 mg/kg group, although overall intubating conditions were similar in the two groups. Suxamethonium-associated muscle pains were significantly more common in the group which received the larger dose ($p < 0.05$).

Key words

Neuromuscular relaxants; suxamethonium.
Complications; myalgia.

Despite the recent introduction of short acting, non-depolarising neuromuscular relaxants, suxamethonium, with its rapid onset of action, complete and predictable paralysis, and short duration of action, remains unsurpassed in providing ideal conditions for the passage of a tracheal tube for short procedures, or when the patient is subsequently to be allowed to breathe spontaneously.[1] However, muscle pains occur frequently in the postoperative period. In 1971 Waters and Mapleson put forward their hypothesis on the aetiology of postsuxamethonium myalgia; they suggested that shearing of soft tissues due to asynchronous muscle contractions was responsible.[2] This work appeared to support the prediction that plotting dose against 'noxious effect' would produce a parabolic curve; pain scores increased in line with suxamethonium dose increase to a peak at a dose of 50–100 mg. The study was neither randomised nor double-blind. Although lower average pain scores were demonstrated in patients receiving lower doses of suxamethonium, it was stated that these doses did not provide adequate relaxation. The present study is a randomised, double-blind comparison of the effects of two doses of suxamethonium, selected from either end of the commonly used range, with regard to intubating conditions and frequency of postoperative muscle pains.

Patients and methods

Sixty-seven patients consented to participate in the study, which had received local ethics committee approval. All the patients were ASA grade 1 adults presenting electively for dental extractions under general anaesthesia. Patients under 16 or over 45 years of age, those where a possible difficulty with intubation was anticipated, or those considered unsuitable to receive the standard anaesthetic technique, were not studied.

None of the patients received sedative premedication. On arrival in the anaesthetic room an intravenous cannula was inserted, ECG monitoring was established, and blood pressure was measured using an automatic sphygmomanometer. Induction of anaesthesia was with intravenous thiopentone 5 mg/kg given over 30 seconds. After a further 30 seconds the dose of suxamethonium (0.5 mg/kg or 1.5 mg/kg diluted to 5 ml with isotonic saline, prepared by a separate investigator according to a random list) was injected over 5 seconds.

One minute after administration of suxamethonium the trachea was intubated under direct laryngoscopy, via the nasal route. Anaesthesia was maintained using nitrous oxide and enflurane in oxygen, with manual ventilation by facemask before intubation, but allowing patients to breathe spontaneously via the tracheal tube when the effects of suxamethonium had worn off.

An assessment of the degree of jaw relaxation, the degree of vocal cord relaxation, and an overall assessment of intubating conditions was made by the anaesthetist according to the scheme adopted by Twohig, Ward and Corall[3] (Tables 1 and 2). Pulse and arterial pressure were measured and recorded automatically before induction, after administration of suxamethonium, one minute after intubation, and 5 minutes after intubation before the beginning of surgery. The time to resumption of spontaneous breathing was also noted.

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Table 1. Classification of grading of intubating conditions.

Jaw relaxation	Good
	Incomplete
	Poor
Cord relaxation	Good, widely abducted.
	Fair, gentle pressure required to pass tube.
	Slight, almost adducted.
	Poor, cords opposed, firm pressure required to pass tube.

Table 2. Grading of overall intubating conditions.

Class	Definition
Excellent	Intubation easy, no reaction from patient.
Good	Intubation resulting in slight coughing or bucking.
Poor	Intubation possible, but resulting in a more marked patient response.

Patients were taken to the recovery area on completion of surgery. Postoperative analgesia was a single dose of intramuscular papaveretum, 0.2–0.3 mg/kg if necessary, plus paracetamol 1 g orally 6 hourly as required.

Patients were followed-up on the first and again on the fourth or fifth day after operation, and were asked about the occurrence and severity of sore throat and muscle pains in a nonleading manner. At the follow-up on the latter occasion, the patient was asked specifically about the nature, severity, site, and duration of postoperative muscle pains. The responses to these questions were assessed and graded (Table 3) by an anaesthetist who did not know to which group the patient belonged.

Statistical analysis was by *t*-test for demographic data, repeated measures analysis of variance for cardiovascular data and Chi-square test with Yates' correction for non-parametric data. Statistical significance was taken as $p<0.05$.

Results

Of the 67 patients who entered the study, full follow-up was achieved in 59 cases (88%). Of these, 27 patients were in the high dose group and 32 patients were in the low dose group. The results from these 59 patients were analysed. There were no significant differences between the groups in age, sex, height, weight, or duration of surgery (Table 4).

Cardiovascular responses to induction and intubation are demonstrated in Figures 1 and 2. Heart rate (Fig. 1) increased on induction in each group of patients, remaining raised after intubation and 5 minutes later. Although the average change in heart rate was the same with each dose, there was a significant dose–time interaction ($p<0.01$). In the high dose group the change from the control value was greater at induction, but less at intubation, when compared with the low dose group. Systolic arterial pressure (Fig. 2) increased in the high dose group on induction, with a further increase following intubation, and a return towards control values by 5 minutes after intubation. By contrast, in the low dose groups, a small reduction in systolic pressure was seen on induction. Although there was an increase in systolic pressure following intubation, this had returned to the control value by the 5 minute measurement. Compared with control values, the increase in systolic arterial pressure was significantly greater ($p<0.01$) in the high dose group at all three assessment times. Diastolic arterial pressure followed a similar pattern in each group, with no significant differences between the groups. There was an increase on induction, with a further rise after intubation, and a return towards the control value 5 minutes later.

Table 3. Grading of severity of muscle pains.

None
Minor, localised to one group of muscles.
Moderate, generalised aches.
Major, interferes with normal activity and mobilisation.

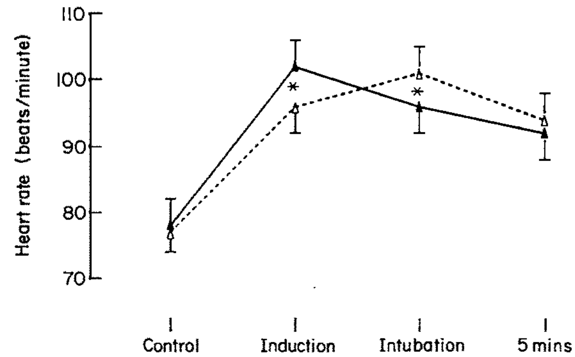

Fig. 1. Changes in heart rate occurring in response to induction and intubation (mean, SEM). ▲——▲, high dose group; △– – –△, low dose group. * increase in heart rate from within group control value is significantly greater on induction in the high dose group and on intubation in the low dose group.

Overall intubating conditions were judged to be similar in the two groups (Table 5). Jaw relaxation was assessed as good in over 90% of patients in each group, and vocal cord relaxation was described as either good or fair in all cases. There were no differences between groups in these respects. Intubation was possible in every case.

Time to resumption of spontaneous breathing was significantly greater in the high dose group with a mean (SD) duration of apnoea of 336 (85) seconds, compared with 227 (77) seconds in the low dose group.

There was no difference between groups in the incidence or severity of postoperative sore throat and, when interviewed after surgery, no patient complained of awareness during anaesthesia. The incidence of post-suxamethonium muscle pains was significantly greater ($p=0.046$) in the high dose group (Table 6). Of the 27 patients in this group from whom responses were obtained, 19 (70%) developed convincing symptoms during the first four days after

Table 4. Demographic data for each group of patients, mean (SD).

	High dose	Low dose
Age; years	24.2 (7.1)	24.5 (7.0)
M:F	9:18	14:18
Height; m	1.60 (0.29)	1.63 (0.29)
Weight; kg	64.2 (17.7)	70.3 (25.7)
Duration of surgery; minutes	21.8 (11.7)	24.8 (9.7)

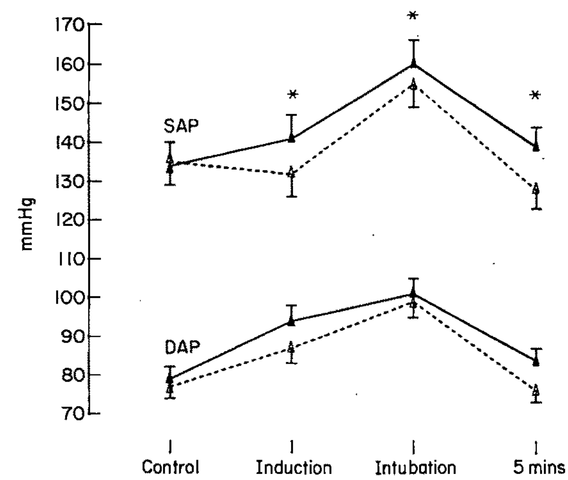

Fig. 2. Changes in systolic arterial pressure (SAP) and diastolic arterial pressure (DAP) occurring in response to induction and intubation (mean, SEM). ▲——▲, high dose group; △– – –△, low dose group. * increase in SAP from within group control value is significantly greater in the high dose group.

surgery. In the low dose group only 13 of the 32 patients (41%) developed symptoms.

Discussion

Although the occurrence of muscle pain following suxamethonium is often listed as a minor side effect, this may be one of the most distressing consequences of minor surgery for the patient. It ranges in severity from a mild ache to disabling discomfort lasting for several days. Of the many regimens which have been proposed as a means to reduce the incidence of this pain, the most effective and widely used method is pretreatment with a small dose of a non-depolarising neuromuscular blocking drug.[4] This technique may give rise to complications, such as difficulty with intubation,[5] and it is recommended that a larger dose of suxamethonium is given to those who are so pretreated.[6] The present study has demonstrated a reduced incidence of pain in patients given a smaller than average dose of suxamethonium. A comparison of low dose suxamethonium against higher dose together with pretreatment using a nondepolarising agent, given to achieve a similar degree of neuromuscular block, would be of interest.

The cardiovascular response to induction of anaesthesia was interesting, with an increase in arterial pressure which was particularly marked in the high dose suxamethonium group. This effect is possibly the result of ganglion stimulation or to noradrenaline release caused by suxamethonium.[7] The dose of thiopentone had been kept to a minimum as there is evidence that thiopentone has a protective effect, reducing the incidence of suxamethonium-associated myalgia.[8] We presume that limiting the dose of induction agent resulted in the hypertensive effect of suxamethonium predominating over the hypotensive effect of thiopentone.

Although slight coughing on intubation was more common in the low dose group, this difference between groups was not statistically significant ($p > 0.1$). It could be argued that the low dose patients may have had incomplete neuromuscular block, either because of dose/response characteristics, or due to delayed onset of action. Although we did not objectively assess neuromuscular block, we have demonstrated that a lower dose of suxamethonium provides clinically adequate intubating conditions for the majority of elective cases. However, when there is a high risk of airway contamination and a rapid sequence induction is to be employed, we would continue to use a larger dose of suxamethonium in an attempt to ensure optimal intubating conditions in every case.

The more prolonged apnoea in the higher dose group was to be expected. This prolongation of apnoea may be particularly important when patients with atypical plasma-cholinesterase are to be anaesthetised. Such patients have been managed with much reduced doses of suxamethonium.[9-11] It would seem logical, when administering suxamethonium, to keep to the minimum effective dose in order to limit the period of apnoea should an unexpected case of this type of suxamethonium sensitivity arise.

In conclusion, we have demonstrated that it is possible to reduce the incidence of suxamethonium-induced muscle pains by restricting the dose administered. This reduction was associated with intubating conditions which were no less favourable than in the group of patients given the higher dose of the drug, and with a less marked cardiovascular response to induction of anaesthesia.

Table 5. Overall intubating conditions.

	High dose	Low dose
Excellent	23	18
Good	3	12
Poor	1	2

Table 6. Occurrence and severity of muscle pains following suxamethonium.

	High dose	Low dose
None	8	19
Minor	4	1
Moderate	11	11
Major	4	1

Acknowledgments

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Anaesthesia, 1991, Volume 46, pages 837–840

Effect of sufentanil on intracranial pressure in neurosurgical patients

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Summary

The effects of sufentanil on intracranial pressure, mean arterial pressure, cerebral perfusion pressure and heart rate were studied in 20 neurosurgical intensive care unit patients. Epidural intracranial pressure probes were implanted in patients who suffered head injury, intracerebral haemorrhage or underwent tumour resection. Sufentanil was given intravenously in sequential doses of 0.5, 1.0 and 2.0 μg/kg. Fifteen minutes elapsed after each dose. The patients were allocated to either group 1 (baseline intracranial pressure < 20 mmHg) or group 2 (baseline intracranial pressure > 20 mmHg). Intracranial pressure did not change significantly in either group. Therefore the falls in mean arterial pressure with the highest dose in both groups and with 1.0 μg/kg in group 2, closely reflect corresponding reductions in cerebral perfusion pressure. As sufentanil in itself exerts no effects on intracranial pressure, concomitant haemodynamic changes are the critical factor for an adequate cerebral perfusion pressure.

Key words

Anaesthesia; neurosurgical.
Analgesics, narcotic; sufentanil.
Measurement techniques; intracranial pressure.
Brain; intracranial pressure, cerebral perfusion pressure.

The absence of any detrimental effects on intracranial pressure is one of the most important features of an ideal anaesthetic for neurosurgical operations and postoperative sedation in the neurosurgical ICU. Fentanyl and sufentanil are thought to be devoid of any adverse effects in patients with space occupying lesions or increased intracranial pressure (ICP),[1] and their use has been advocated for neurosurgical procedures.[2,3] Additionally, because of their great cardiovascular stability[4] and stress suppressing capacity[5] they seemed suitable for providing sedation in the neurosurgical ICU.

The elimination half-life of sufentanil is shorter than that of fentanyl and the high tissue affinity reflects the lipophilic nature of this drug.[6] However, the widespread use of sufentanil for this patient population has recently been challenged by a number of investigations which indicate a detrimental effect of this agent in patients at risk of increased ICP. Milde[7] reported that sufentanil over a wide range of dosage is a potent cerebral vasodilator and increases cerebral blood flow (CBF) in dogs. Marx[8] found similar results in humans anaesthetised with a thiopentone–nitrous oxide–vecuronium sequence (ICP measured with a lumbar subarachnoid catheter). In contrast, a study on primates by Bunegin *et al.* showed only a mild effect of sufentanil on intracerebral pressure.[9] The current controversy prompted us to investigate the effects of sufentanil on ICP in our patients at the neurosurgical ICU.

Methods

An epidural ICP probe (Gaeltec)[10] was implanted in a total of 20 neurosurgical ICU patients with head injury, intracerebral haemorrhage or after tumour resection, after approval by the institutional committee on human research, and informed consent (see Tables 1 and 2). The transducer was implanted in the operating theatre following the neurosurgical procedure.

All patients were sedated with midazolam 0.1 mg/kg/hour and sufentanil 1 μg/kg/hour. Sufentanil administration was stopped 5 hours before data were recorded, twice the elimination half-life of 164 (SD22) minutes.[6] Midazolam infusion was stopped one hour before measurements were made. Sufentanil was given in incremental dosages of 0.5 μg/kg, 1.0 μg/kg and 2.0 μg/kg with 15-minute intervals between doses. Heart rate, systolic pressure, diastolic pressure, mean arterial pressure (MAP) and intracranial pressure (ICP) were monitored continu-

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Table 1. Clinical characteristics and diagnosis in group 1 patients.

Patient No.	Age, years	Sex	Diagnosis
1	26	Female	Intracerebral haemorrhage
2	45	Male	Subdural haematoma
3	22	Male	Angioma bleeding
4	43	Female	Intracerebral haemorrhage
5	33	Female	Subarachnoid haemorrhage
6	22	Male	Epidural haematoma
5	53	Male	Subarachnoid haemorrhage
8	61	Male	Meningioma
9	58	Male	Pituitary adenoma
10	38	Female	Epidural haematoma
11	67	Male	Epidural haematoma

The mean age of group 1 patients was 42 (SEM, 5) years.

Table 2. Clinical characteristics and diagnosis in group 2 patients.

Patient No.	Age, years	Sex	Diagnosis
1	60	Female	Intracerebral haemorrhage
2	22	Male	Epidural haematoma
3	45	Male	Intracerebral haemorrhage
4	68	Male	Meningioma
5	43	Male	Intracerebral haemorrhage
6	38	Male	Sudural haematoma
7	55	Female	Angioma bleeding
8	43	Male	Subdural haematoma
9	35	Male	Intracerebral haemorrhage

The mean age of group 2 patients was 45 (SEM, 5) years.

ously and recorded on an integrated data bank (Hewlett-Packard 758534A). Data were evaluated 2 and 5 minutes after each administration. Since there were no significant differences in the measured variables i.e. 2 and 5 minutes after each sufentanil administration, the respective data were pooled. Furthermore, monitoring of end-tidal CO_2 (Hewlett-Packard 75834A) guaranteed constant $P\text{CO}_2$ values within the range of 4 to 4.67 kPa. Cerebral perfusion pressure (CPP) was calculated as the difference between mean arterial pressure and ICP. Patients were allocated either to group 1 (ICP < 20 mmHg, 11 patients) or group 2 (ICP > 20 mmHg, nine patients) according to their baseline ICP level. Statistical significance was calculated by one-way ANOVA with post hoc comparisons by Fisher's 'protected least significant difference'. A p value of < 0.05 was regarded as significant.

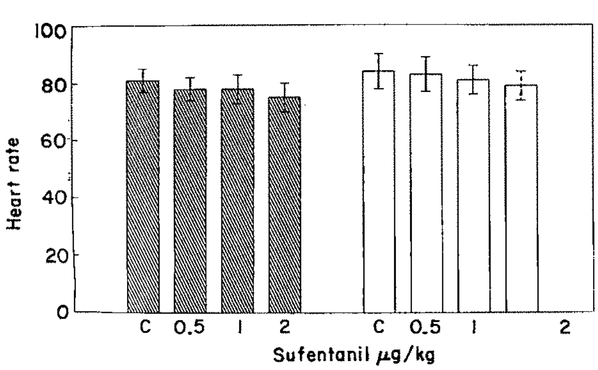

Fig. 1. Changes in heart rate after administration of sufentanil did not reach significant levels. Values of group 1 patients are depicted as hatched bars, those of group 2 as open bars (means, SEM).

Results

A mild decrease could be observed in the heart rates of both groups, as presented in Figure 1, but changes did not reach significance. Proportions of mean arterial pressure, intracerebral pressure and cerebral perfusion pressure are

Table 3. Changes in MAP, ICP and CPP (in mmHg) in group 1 after administration of sufentanil, mean (SEM).

		Sufentanil (µg/kg)		
	Control	0.5	1.0	2.0
HR	81(4)	78(4)	78(5)	75(5)
MAP	78(4)	74(4)	77(5)	71(3)*
ICP	12(2)	12(2)	11(1)	12(1)
CPP	65(5)	62(5)	65(5)	60(3)*

*$p < 0.05$.

Table 4. Changes in MAP, ICP and CPP (in mmHg) in group 2 after administration of sufentanil, mean (SEM).

		Sufentanil (µg/kg)		
	Control	0.5	1.0	2.0
HR	84(6)	83(6)	82(5)	79(5)
MAP	91(6)	84(4)	79(3)*	76(3)*
ICP	30(2)	31(3)	29(2)	29(2)
CPP	60(5)	53(4)	49(3)*	47(3)*

*$p < 0.05$.

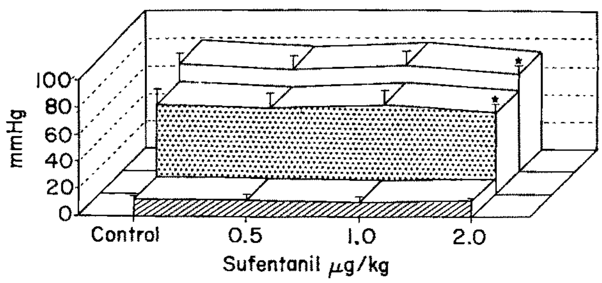

Fig. 2. Effect of sufentanil on MAP (□), ICP (▨) and CPP (▤) in group 1 patients ($n = 11$). Significant changes in MAP and CPP appeared only after 2.0 μg/kg sufentanil. Mean, SEM; $^*p < 0.05$.

shown in Figure 2. This represents group 1 patients with ICP values of up to 20 mmHg while Figure 3 represents group 2 patients with ICP values over 20 mmHg. In group 1, a significant decrease in MAP and CPP was seen only after the 2.0 μg/kg dosage. No significant difference in MAP and CPP was noted with sufentanil 0.5 and 1.0 μg/kg. ICP remained stable throughout in group 1.

Significant decreases in MAP with sufentanil 1.0 and 2.0 μg/kg closely reflected corresponding CPP alterations in group 2. Mean cerebral perfusion pressure after administration of sufentanil 1.0 μg/kg (49 (SEM) 3 mmHg) and 2.0 μg/kg (47 (SEM) 3 mmHg) decreased significantly. There was no difference in the measured ICP readings compared to the control value in group 2.

Discussion

Sufentanil is an opioid analgesic 5–10 times as potent as fentanyl[11] and has a favourable effect on the CNS, similar to other morphine-like drugs.[12] The decrease in MAP that we demonstrated is probably the result of peripherial vasodilation due to sufentanil, since its previous administration was 5 hours before. In both groups ICP remained stable with all doses. Decreases in CPP were the result of lowering MAP. These results are in contrast to Milde's study[7] who found sufentanil detrimental to reduced intracranial compliance because of an increase in cerebral blood flow in anaesthetised dogs following doses of 2 to 200 μg/kg. Milde concluded that sufentanil is a potent cerebral vasodilator. This study can be criticised because dogs' susceptibility to opioids is known to be different from humans'.[13] Moreover, N_2O in combination with halothane increases cerebrospinal fluid pressure (CSFP).[14,15] We did not use N_2O and had stopped infusing sufentanil and midazolam long before data were collected. Marx showed that in comparison with fentanyl, and alfentanil sufentanil caused the greatest increase of CSFP in patients with brain tumours.[8] Our findings of unchanged ICP in both groups conform with the findings of Bunegin *et al.*[9] who investigated cerebrovascular responses to sufentanil in Rhesus monkeys, in whom ICP did not change significantly with normal or elevated ICP. In addition, we have shown previously that sufentanil does not change cerebral blood flow or cerebral vascular resistance significantly in humans.[16] All patients were mildly hyperventilated because of the effect of $P\text{CO}_2$ on ICP and CBF; this prevented increased ICP because of hypercarbia.[17,18]

In conclusion, sufentanil in doses of up to 2.0 μg/kg and in a cumulative dose of 3.5 μg/kg, has no significant effect on ICP in neurosurgical patients with normal or decreased intracranial compliance. Patients with elevated ICP seem to be more sensitive to the haemodynamic effects of sufentanil, although decreases in cerebral perfusion pressure were confined to the highest dose studied.

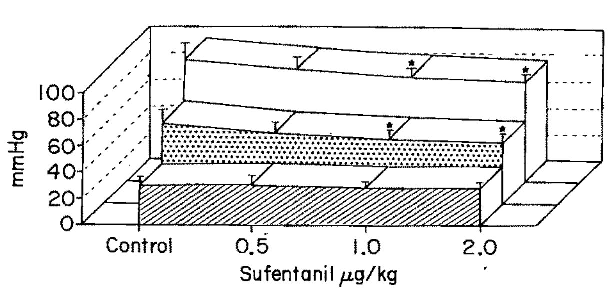

Fig. 3. Effect of sufentanil on MAP, ICP and CPP in group 2 patients ($n = 9$). Significant changes in MAP (□) and CPP (▤) appeared after 1.0 μg/kg as well as after 2.0 μg/kg. ICP (▨) remained stable. Mean, SEM. $^*p < 0.05$.

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Posterior tibial nerve block

A new approach using the bony landmark of the sustentaculum tali

M. R. WASSEF

Summary

A local analgesic block of the posterior tibial nerve, using a new subcalcaneal approach, is described. The point of insertion of the needle is defined in relation to a bony prominence below the medial malleolus, the sustentaculum tali, to which the posterior tibial nerve bears a constant relationship. Twenty patients given a posterior tibial block using the subcalcaneal approach were compared with 20 patients in whom a traditional retrotibial approach was used. In this technique the major landmark for needle insertion is the posterior tibial artery. In all patients the techniques formed part of an ankle block for foot surgery. Eighty-five to 90% of patients had peripheral vascular disease and in 60–65% the posterior tibial artery was not palpable. In the group of patients without palpable pulses, the subcalcaneal approach had a success rate of 100%, whereas all those having the retrotibial approach required additional local analgesic supplements ($p < 0.001$)*. The subcalcaneal approach is simple and is particularly recommended for patients with peripheral vascular disease.*

Key words

Anaesthetic techniques, regional; ankle.
Nerve; posterior tibial.

An ankle block is a form of regional analgesic technique with which some operations on the foot may be performed. It entails blockade of the superficial and deep peroneal nerves which supply the dorsum of the foot, the sural nerve which supplies the lateral aspect of the foot, the saphenous nerve for the posteromedial aspect of the foot and the posterior tibial nerve for the sole of the foot. Blockade of the posterior tibial nerve has been described in many text books. All the approaches to the nerve are in the region of the ankle joint, but are subject to slight variations in approach with respect to the patient's posture, landmarks used, site and direction of needle insertion and volume of local analgesic required. The landmarks used are rather imprecise and this factor contributes to inaccuracies of needle placement and an incidence of block failure. Many techniques depend on the posterior tibial artery as a landmark, but in some patients this is not palpable. In this paper, a new approach to the posterior tibial nerve is described.

Anatomical perspective

In the distal part of the leg, the posterior tibial nerve, together with the posterior tibial artery, lies about midway between the tendo Achillis and the posteromedial border of the tibia. It lies in an area filled with fibrofatty tissue[1] and curves along the medial side of the calcaneum, where it lies medial to the posterior tibial artery. Both structures run first behind, then underneath the sustentaculum tali, where they divide into medial and lateral plantar branches, which supply the sole of the foot. The sustentaculum tali is a projecting shelf on the medial side of the calcaneum, (Fig. 1) which can be palpated 2–3 cm below the medial malleolus of the tibia.[2]

Methods

Forty ASA 1–3 patients scheduled for elective foot surgery were divided into two groups. Group A ($n = 20$) received an ankle block in which the subcalcaneal approach to the posterior tibial nerve was used. Group B ($n = 20$) received an ankle block using the traditional approach to the posterior tibial nerve. This work was undertaken in accordance with our institutional policy. Each patient received 0.5–1.0 mg of midazolam intravenously for sedation before the technique was performed.

The subcalcaneal approach

With the patient in the supine position, the foot is externally rotated. The tip of the medial malleolus is identified

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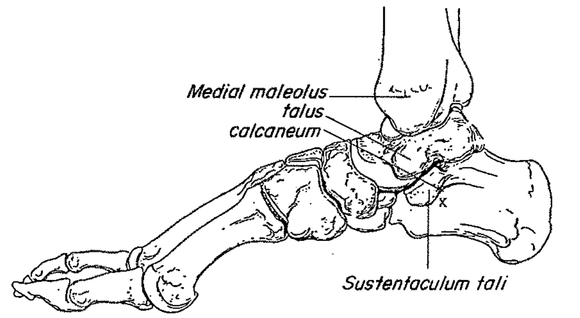

Fig. 1. Medial aspect of the skeleton of the foot showing the sustentaculum tali. x indicates the point of entry of the needle for the subcalcaneal approach to the posterior tibial nerve.

and the palpating finger is moved perpendicularly downwards until a bony ridge, the sustentaculum tali, is identified. A 22-gauge 3.2 cm needle is introduced at a point immediately posterior and inferior to the ridge (Fig. 1). This point lies on a perpendicular line drawn downwards from the midpoint of the tip of the medial malleolus. The needle is inserted until bone is felt, then withdrawn about 2 mm. Three to five ml of 2.0% lignocaine with 1 : 200 000 adrenaline is injected after a negative aspiration test. It is not necessary to elicit paraesthesiae.

The retrotibial approach

With the patient in the supine position, the foot is raised on a folded towel and externally rotated. A 22-gauge 3.2-cm needle is inserted at the midpoint of a line joining the tendo Achillis and the upper end of the medial malleolus. The needle is directed anterolaterally until the posterior surface of tibia is felt, then withdrawn for 2–3 mm and 5–10 ml of 2.0% lignocaine with 1 : 200 000 adrenaline is injected after a negative aspiration test.

All patients received the posterior tibial nerve block first. The degree of patient discomfort, in terms of pain perceived in relation to this block, was then immediately assessed as minimal, mild, moderate or severe. This was followed by blockade of the remaining nerves to complete the ankle block. Each patient was examined for the presence or absence of posterior artery pulsation. The result of the posterior tibial nerve block was assessed in both groups in terms of complete or partial success.

Whenever a patient complained of pain related to the posterior tibial nerve distribution, during the course of the operation, a supplement of local anaesthetic or an intravenous narcotic agent was administered. Patient satisfaction was also assessed. Each patient was asked to state whether he (she) was completely satisfied with the nerve block, had minor or major reservations, or was dissatisfied with it.

Student's *t*-test and the Chi-squared test were used for statistical analysis, where appropriate, with the level of significance taken as $p < 0.05$.

Table 1. Demographic data of patients.

	Group A subcalcaneal approach	Group B retrotibial approach
Patients	$n=20$	$n=20$
Age; years, mean (SE)	55.35 (2.52)	53.80 (2.79)
Range; years	27–72	25–70
Weight; kg, mean (SE)	70.50 (1.77)	67.10 (1.46)
Range; kg	53–79	56–76
Sex ratio (M : F)	16 : 4	16 : 4
Volume of lignocaine, ml mean (SE)	3.50 (0.19)*	8.40 (0.48)*
Range; ml	3.00–5.00	5.00–10.0

SE = Standard error of the mean.
*$p<0.001$.

Table 2. Distribution of nature of operation, peripheral vascular disease and absence of posterior tibial artery pulsations between the groups.

	Group A subcalcaneal approach	Group B retrotibial approach
Foreign body removal	10.00% ($n=2$)	15.00% ($n=3$)
Distal amputation	90.00% ($n=18$)	85.00% ($n=17$)
Peripheral vascular disease	90.00% ($n=18$)	85.00% ($n=17$)
Absent pulsations	65.00% ($n=13$)	60.00% ($n=12$)

Results

The subjects in the two groups were comparable with respect to age, weight and sex distribution (Table 1). The volume of local analgesic used in the subcalcaneal patients (3–5 ml) was significantly lower than that used in the retrotibial patients (5–10 ml), $p < 0.001$.

The nature of the surgery was also comparable in both groups (Table 2). Foreign body removal was performed in 10–15% of patients, while 85–90% had peripheral vascular disease and underwent some form of distal amputation of either the toes or distal part of the metatarsals.

The subcalcaneal approach was completely successful in all patients. In those patients who had the retrotibial approach, only 30% had a completely successful block. Sixty-five percent required local analgesic supplementation

Table 3. Percentage outcome of posterior tibial nerve block, for patients undergoing subcalcaneal (group A) or retrotibial (group B) approaches.

	Success	Local analgesic supplement required	Intravenous narcotic required
Group A	100.0% ($n=20$)*	00*	00*
Pulseless patients	100.0% ($n=13$)*	00*	00
Group B	30.0% ($n=6$)*	65.0% ($n=13$)*	5.0% ($n=1$)*
Pulseless patients	00	100.0% ($n=12$)*	00

*$p<0.001$.

Table 4. Degree of patient discomfort associated with block for patients undergoing subcalcaneal (group A) or retrotibial (group B) approaches. Percentage of number in each group.

	Minimal	Mild	Moderate	Severe
Subcalcaneal (A)	95.0%*	5.0%*	0*	0
Number of patients	19	1	0	0
Retrotibial (B)	50.0%*	30.0%*	20.0%*	0
Number of patients	10	6	4	0

*p<0.05.

and 5% required an intravenous analgesic, $p < 0.001$, (Table 3).

In 60–65% of patients the posterior tibial artery was not palpable. The subcalcaneal approach was successful in all patients without tibial pulses, whereas the retrotibial approach was unsuccessful in this group of patients, all of whom required local analgesic supplementation ($p < 0.001$).

The patients in the subcalcaneal group had significantly less discomfort and expressed significantly greater overall satisfaction with the block than those in the retrotibial group ($p < 0.02$).

All patients remained stable intra-operatively and no neurological or other complications occurred in the post-operative period.

Discussion

In this study of patients having ankle blocks, the success rate of the posterior tibial nerve block performed using the subcalcaneal approach was 100%, whereas that using the traditional retrotibial approach was only 30%. In the retrotibial group of patients 65% required local analgesic supplementation. Patients in the subcalcaneal group experienced less discomfort, and found the block more acceptable.

Despite the variations in approach to the posterior tibial nerve described in text books of regional anaesthesia, all are restricted essentially to the posteromedial aspect of the ankle joint. Atkinson *et al.*[3] and Bridenbaugh[4] advocate the prone position. In the technique described by Atkinson *et al.* the needle is inserted at a point just internal to the tendo-Achillis and deep to the flexor retinaculum near the posterior tibial artery (if palpable). The needle is then directed forwards and laterally, close to the posterior surface of the tibia. In Bridenbaugh's technique the needle is inserted lateral to the posterior tibial artery or medial to the tendo Achillis at the upper border of the medial malleolus, and directed at right angles to the posterior surface of the tibia. In contrast, the lateral decubitus position is recommended by Katz[5] and Carron.[6] The former directs the needle towards the posterior tibial artery. The latter

Fig. 2. X ray of the medial aspect of the foot, showing the spread of local analgesic behind and below the sustentaculum tali.

inserts the needle through a point at the level of the superior border of the medial malleolus, midway between it and the tendo-Achillis, and directed forwards towards the second toe. All these authors used 5–10 ml of local analgesic.

A midtarsal block for forefoot surgery has been described recently.[7] In this technique the posterior tibial nerve can be blocked with the patient in the supine position. The posterior tibial artery provides a landmark as it courses between the medial malleolus and the heel. At this point the nerve is quite superficial, so it can be located accurately and a smaller volume of local analgesic may be used.

The subcalcaneal approach to posterior tibial nerve blockade described in this paper is a new technique. The needle is inserted behind and below a bony protuberence, on the medial aspect of the calcaneum, the sustentaculum tali (Fig. 1). The posterior tibial nerve bears a constant anatomical relationship to this bony landmark. Figure 2 shows an X ray of the foot after the block has been performed. Local analgesic mixed with a radiopaque substance is seen bathing the course of the posterior tibial nerve, starting from behind the tibia and coursing immediately behind and below the sustentaculum tali, reaching the sole of the foot.

The majority of patients (85–90%) were scheduled for some form of amputation of the distal part of the foot. Sixty to 65% of all patients suffered from peripheral

Table 5. Degree of overall patient satisfaction with subcalcaneal (group A) or retrotibial (group B) approaches to posterior tibial nerve block. Percentage of number in each group.

	Complete satisfaction	Minor reservation	Major reservation	Dissatisfaction
Subcalcaneal (A)	95.0% (n=19)*	5.0% (n=1)*	0*	0
Retrotibial (B)	50.0% (n=10)*	30.0% (n=6)*	20.0% (n=4)*	0

*p<0.02.

vascular disease and the posterior tibial artery was impalpable. This artery therefore could not be used as a landmark for determining the point of entry of the needle. This might explain the 70% failure rate in patients who received the retrotibial approach, and the 100% failure rate in patients with absent posterior tibial artery pulsations. The subcalcaneal approach to the posterior tibial nerve block was 100% successful, irrespective of the ability to palpate the posterior tibial artery.

In conclusion, the subcalcaneal approach to posterior tibial nerve blockade is a new technique that offers certain anatomical advantages compared with traditional techniques. First of all, at this point, the posterior tibial nerve is very superficial. Secondly, the nerve bears a constant and close relationship to the sustentaculum tali, an easily palpable bony protuberance underneath the medial malleolus. Finally, the high success rate in patients with impalpable posterior tibial artery pulsations makes the new technique particularly useful for patients with peripheral vascular disease.

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Are you getting the message?

A look at the communication between the Department of Health, manufacturers and anaesthetists

P. M. WEIR AND M. E. WILSON

Summary

A questionnaire sent to 109 anaesthetists in the South West Region has revealed that there is a problem with dissemination of information relating to hazards with equipment. Thirty-four per cent of consultants, and 67% of junior anaesthetists were only slightly or not at all confident that they see the Hazard Notices and Safety Action Bulletins relating to the equipment they use. The study has also demonstrated the large amount of new equipment coming into circulation and has highlighted deficiencies in the reading of equipment manuals. Some suggestions are made as to how the current system may be improved.

Key words

Equipment.
Anaesthesia audit.

This study was undertaken because of a fear that anaesthetists often do not receive official warning notices and do not read equipment manuals. It also provided an opportunity to find out what new equipment had been obtained during the previous year and what journals are read.

Method

A questionnaire (Fig. 1) was sent to every third anaesthetist chosen at random from within their department in the South West Region. First we asked if anaesthetists were confident that they saw Hazard Notices and Safety Action Bulletins (SAB) relating to the equipment they use. Then we asked if the method of reporting a problem, within their own department and from other units, was satisfactory and how they would nationally report a serious mishap.

Next we asked if a new piece of equipment had been used in the last year and if so whether the respondents had read the manual and how useful they found it. We also asked if they followed the manufacturer's checking procedure before using equipment.

Respondents were questioned about whether they were aware of any Department of Health publications relevant to anaesthesia and which anaesthetic journals they read. They were also given the opportunity to suggest how the current system could be improved.

Results

Eighty-nine replies were received from the 109 questionnaires sent out (82% response rate). Of these, 44 replies were from consultants and 45 from junior anaesthetists (11 Senior Registrars, 15 Registrars, 17 SHOs and two Others).

Table 1 shows how confident anaesthetists were that they saw Hazard Notices and Safety Action Bulletins relating to anaesthesia. Of the 17 juniors who were not at all confident six were senior registrars. Overall 26 (59%) consultants and 13 (29%) juniors felt that the current system for bringing these notices to the attention of the relevant staff was satisfactory in their hospital.

When asked how they would nationally report a serious mishap 15/26 (58%) consultants and 2/27 (7%) juniors said they would contact the Department of Health. Of the 11 consultants who gave alternative answers four said they

Table 1. Anaesthetists' confidence that they had seen Hazard Notices and Safety Action Bulletins.

	Consultants	Juniors
Very confident	7 (16%)	1 (2%)
Moderately confident	22 (50%)	14 (31%)
Slightly confident	4 (9%)	13 (29%)
Not at all confident	11 (25%)	17 (38%)
Totals	44	45

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Are your getting the message?

1 (a) How confident are you that you see all the Hazard Notices and Safety Action Bulletins relating to the equipment that you use?

Very Moderately Slightly Not at all

(b) Do you consider that the system in your hospital for bringing these to the attention of the appropriate staff is satisfactory?

Yes No

(b) If No, how do you think this could be improved?

2 (a) If you have a problem with a piece of equipment in your hospital is the method of reporting this problem within your department satisfactory?

Yes No

(b) If No, how do you think this could be improved?

3 Please delete as appropriate.

	ANAESTHETIC MACHINE	SEPARATE VENTILATOR	SEPARATE MONITOR
In the past year have you used a new item of equipment?	Y/N	Y/N	Y/N
If Yes, state make and model:			
Did you find the manual useful?	Very/moderately slightly/not at all/ didn't read	Very/moderately/ slightly/not at all/ didn't read	Very/moderately/ slightly/not at all/ didn't read
If you did not find the manual useful why was that?			
Before use do you follow the manufacturer's checking procedure?	Y/N	Y/N	Y/N
If No why not?			

4 Are you aware of any Department of Health publications that are of special importance to anaesthesia?

Yes No

If Yes, please specify.

5 Grade of anaesthetist Consultant Senior Registrar Registrar Senior House Officer Other

6 Are you involved in the purchasing of equipment?

Yes No

If Yes, has any publication been useful in making your choice?

7 Do you read the following journals?

	Nearly always	Usually	Often	Seldom	Never
Anaesthesia					
British Journal of Anaesthesia					
**European Journal of Anaesthesia*					
Anaesthesia and Intensive Care					
Canadian Journal of Anaesthesia					
Acta Anaesthesiologica Scandinavica					
Anesthesiology					
Anesthesia and Analgesia					

8 Thank you very much for taking the time to fill in this questionnaire. If you would like to have a copy of the results of this survey please tick the box and put your name and address underneath.

* The *European Journal of Anaesthesia* was subsequently excluded since it is no longer published.

Fig. 1.

Table 2. Experiences of anaesthetists with manuals.

Usefulness of manual	Consultants	Juniors
Very useful	11 (16%)	8 (10%)
Moderately useful	19 (28%)	22 (27%)
Slightly useful	5 (7%)	10 (12%)
Not at all useful	0	2 (2.5%)
Did not read	33 (48%)	38 (47%)
Total	68	80

would go via a head of department, two via local safety officers, four via journals and one did not know what to do.

The internal reporting of equipment problems was considered satisfactory by 40 (91%) consultants and 32 (71%) juniors.

All but three consultants and two juniors had used a new piece of equipment within the last year. There were 151 reports of the acquisition of new equipment (predominantly anaesthetic machines and monitoring equipment). Consultants used 70 and juniors 81 new items. Their experiences with the manual are shown in Table 2.

The main reasons stated for not using the manual were: too complicated or too long (10), did not contain enough information (4) or not available (7).

On 40% of occasions anaesthetists followed the manufacturer's checking procedure for new equipment. Reasons for not doing so were: own drill preferred, reliance on ODAs, ignorance of manufacturer's procedure or that the recommended check took too long. Many anaesthetists felt that the manufacturer's checking procedure for monitors was unnecessary—a little common sense was all that was required.

Only 28 (64%) consultants knew of any Department of Health publication relevant to anaesthesia. Those cited were predominantly Health Equipment Information Bulletins (HEIs), Hazard Warning Notices or Safety Action Bulletins. Only 11 of the juniors were able to name any such publication (four senior registrars, six registrars, one senior house officer). Out of 17 consultants involved in equipment purchase only 13 knew of HEIs; eight of these found that a publication had been useful in choosing equipment.

Table 3 shows the frequency with which the most well known anaesthetic journals are read.

Discussion

These results have confirmed our suspicions and those of others[1] that information about the safe use of anaesthetic equipment is poorly communicated.

Overall, two-thirds of junior anaesthetists and one-third of consultants were not at all confident, or were only slightly confident, that they had seen the relevant Hazard Notices and Safety Action Bulletins. The existing mechanism depends upon a final distribution by the health authorities. This can be carried out economically by the Department of Health (D of H) and it allows irrelevant notices, referring to equipment not possessed by a particular department, to be sifted out. However, we provide evidence that the health authorities cannot be relied upon to complete the distribution to all anaesthetists (and, we suspect, to their technical support staff—maintenance engineers, Operating Department Assistants, and anaesthetic nurses). It appears that even if notices reach departmental heads there is no assurance that they will be prominently displayed or publicised at departmental meetings. The dull civil service format of these notices compounds the problem. Safety Action Bulletins are also publicised in *Anaesthesia* but it appears that this does not ensure that the notices are read, despite 88% of our correspondents regularly reading the journal (Table 3). Several respondents suggested that departments should appoint a safety coordinator to ensure that notices are drawn to the attention of all concerned. Another suggestion was that the D of H should mail notices directly to anaesthetists, as is done by the Committee of Safety in Medicines (CSM) and the Chief Medical Officer. We strongly support these suggestions.

Anaesthetists, especially junior ones, appear confused about the best way to report a faulty piece of equipment. Official guidance is poor. The NHS Procurement Directorate, which investigates serious incidents, is the appropriate body but it does not advertise and encourage reporting in the same way that the CSM does in its 'Yellow Card' system for adverse drug reaction. We suspect most anaesthetists, like us, were unaware of HC(88)51, until the 'Reminder to report incidents in accordance with HC(88)51' was published in *Anaesthesia*.[2] Hitherto anaesthetists may well have been confused by the alternatives. Should a report be sent to the manufacturers, or can the D of H be relied upon to do this? Should a report be sent to

Table 3. Frequency of reading of anaesthetic journals.

	Percentage reading journal				
Journal	Nearly always	Usually	Often	Seldom	Never
Anaesthesia	76%	12.5%	2.5%	7.5%	1%
British Journal of Anaesthesia	59%	15%	15%	11%	0
Anesthesiology	11%	11%	29%	32.5%	16%
Anesthesia and Analgesia	7.5%	7.5%	16%	39%	30%
Anaesthesia and Intensive Care	7.5%	6%	15%	56%	15%
Canadian Journal of Anaesthesia	1%	9%	7.5%	45%	37.5%
Acta Anaesthesiologica Scandinavica	0	4%	7.5%	47.5%	41%

the Safety Committee of the Association of Anaesthetists? (Indeed what is the function of this committee)? Should an attempt be made to publish a description of the incident in a journal? Seventeen out of 53 anaesthetists in our study would report an incident directly to the D of H and a further 13/53 would report to their head of department (presumably expecting it to be forwarded to the D of H). There remains 40% of anaesthetists who would depend upon other routes, principally the slow and uncertain mechanism of writing a report to one of the journals.

The questionnaire highlighted the large amount of equipment coming into circulation, and noted that all but a handful of anaesthetists used a new piece of equipment in the last year. Therefore it is essential that good manuals and check procedures are provided as the basis of a training programme.

Failure to understand equipment is a well recognised cause of critical incidents or anaesthetic deaths. However, we found that half the anaesthetists had not read the manuals (six said they were satisfied with manufacturer's demonstrations and seven could not find the manuals). Only 13% of those who had read the manuals found them to be very useful. We believe that these disappointing results reflect the fact that many manuals are badly written with little thought given to the requirements of the anaesthetist. Manuals for machines have become dauntingly large (one runs to two volumes) with some sections containing unduly lengthy and obvious statements. The contents are seldom arranged to provide the new user with ready access to a quick working guide at the front of the manual. A simple account of how the equipment works is rarely included. Research and development should not be confined to the engineers. We suggest manufacturers pay more attention to their manuals to ensure that equipment is properly understood and safely used.

Failure to check equipment is also known to be a frequent cause of critical incidents or anaesthetic deaths. It seems reasonable to suppose that the manufacturer is best able to devise a suitable check procedure for an item of equipment, yet only about a third of anaesthetists followed their recommendations. The less acceptable excuses for failure to use the manufacturer's check were ignorance of them and reliance on assistants to do the work.

Understandably, many anaesthetists were critical of lengthy check lists and preferred their own system. Our own main criticisms of manufacturer's checks are that they are often unrealistic, apparently being devised to suit lawyers rather than busy anaesthetists. We also find many items too unspecific to be useful (e.g. 'check the integrity of . . .' without explaining how this is to be achieved).

It should be a cause for concern that only two out of three consultant anaesthetists, and far fewer juniors, are aware of the HEIs. A higher proportion (76%) of anaesthetists involved in the purchase of equipment read these publications, but only 47% of consultants found them useful when choosing equipment. This is a disappointing finding considering the amount of work that goes into the research and collection of information by the D of H to encourage a discerning approach to the purchase of equipment.

This study also reveals a gap in the training provided to junior anaesthetists. It appears that they are not required to read manuals or follow check procedures. Many are ignorant of the procedures for reporting incidents and are unaware of useful D of H publications, and are also no doubt unaware of relevant British Standard and International Standard publications.

In conclusion, we suggest that to improve anaesthetic safety a greater attempt should be made to ensure that warning notices and manuals are properly read by the users. To achieve this, they must (a) appear important, (b) be sensibly written, (c) reach the target audience. We present evidence that all too often manufacturer's instructions and D of H warnings do not achieve these requirements and so fail to make the necessary impact. There can be no doubt about their importance. Unfortunately their style and content may not encourage anaesthetists to study them. Finally, and most importantly, we have exposed serious weaknesses in the chain of communications especially between the anaesthetist and the D of H.

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CASE REPORT

Postoperative obstructive sleep apnoea

Haemodynamic effects of treatment with nasal CPAP

M. K. REEDER, M. D. GOLDMAN, L. LOH, A. D. MUIR, K. R. CASEY AND D. A. GITLIN

Summary

A 74-year-old man presenting for aortic reconstructive surgery showed severe, previously undiagnosed obstructive sleep apnoea during overnight oximetry monitoring before operation. Postoperatively, in the first 4 hours following extubation, he suffered 238 episodes of respiratory obstruction. These events were associated with frequent arousals, large fluctuations in systolic and diastolic blood pressure. Administration of nasal continuous positive airways pressure abolished the obstructions and allowed an uninterrupted night's sleep, with a significantly reduced blood pressure. Subsequent dips in oxygen saturation as a result of respiratory obstruction recurred on the fifth postoperative night. We conclude that pre-operative overnight oximetry may be useful in identifying those patients at risk of postoperative upper airway obstruction. Use of nasal continuous positive airway pressure may prevent the occurrence of early postoperative obstruction and the associated haemodynamic changes.

Key words

Complications; sleep apnoea.
Ventilation; continuous positive pressure.

Frequent episodic reductions in arterial oxygen saturation ($Sa{O_2}$) have been observed in normal patients with intravenous opioid infusions during the first 16 hours after surgery, and are related to complete or partial respiratory obstruction.[1] Similar episodes have been reported during the first 48 hours following surgery.[2] We report a case of previously undiagnosed obstructive sleep apnoea, in which severe episodic respiratory obstructions occurred both early and late in the postoperative period. The haemodynamic changes accompanying early episodes of respiratory obstruction and the effect of nasal continuous positive airway pressure (CPAP) are reported.

Methods

The patient was studied in an investigation of pre- and postoperative levels of arterial oxygen saturation in patients undergoing elective major abdominal vascular surgery. Data for $Sa{O_2}$ and heart rate were sampled once each second from the digital output (RS-232) of an Ohmeda 3700 pulse oximeter, using a computer program designed for respiratory sleep studies. Data were redisplayed and plotted graphically against time. On the first postoperative night, blood pressure was recorded noninvasively from a Finapres 2300 (Ohmeda). The digital output of the Finapres (systolic, diastolic mean BP and heart rate) was sampled each beat by a microcomputer simultaneously with $Sa{O_2}$ data from the oximeter.

On the pre-operative night oxygen saturation and heart rate alone were recorded. On the first postoperative night, the patient's respiratory effort was assessed by the pressure changes occurring in an intra-oesophageal balloon, and airflow was detected using nasal and oral thermistors. The signals from these were displayed by a Kontron Colormon ITU monitor and then recorded directly onto VHS video tape. Detailed analysis of airflow and respiratory effort was made by replaying the tape.

Case history

A 74-year-old man, weight 93 kg and height 174 cm, was admitted to hospital bleeding from an aorto-duodenal fistula. He had previously undergone an aortic tube graft for an inflammatory aortic aneurysm. Although overweight he had no history of respiratory or cardiovascular disease. However, on later questioning, a history of heavy snoring was obtained from the patient and confirmed by his wife.

Pre-operative overnight pulse oximetry

There were 295 episodes of desaturation greater than 4% during the pre-operative night (36 events per hour). Many

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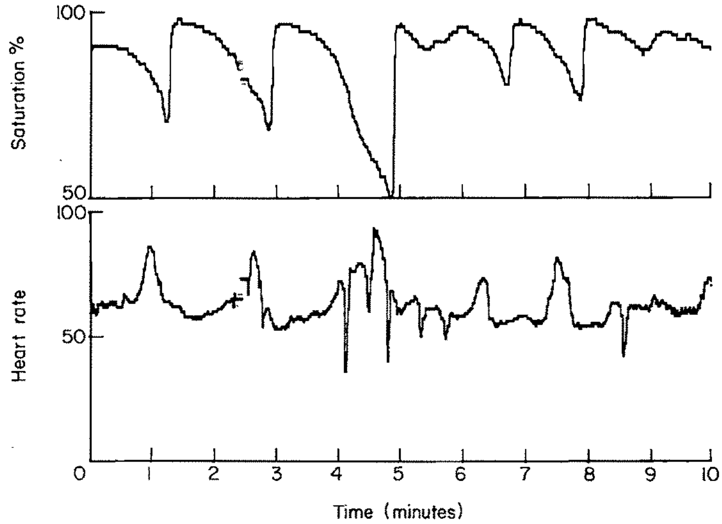

Fig. 1. Pre-operative overnight oximetry study. Typical 10-minute tracing of oxygen saturation and heart rate during periodic upper airway obstruction. Note the relatively slow desaturation phase with rapid resaturation and increase in heart rate upon relief of obstruction.

episodes were severe with 30 dips to values below 80% saturation. A typical 30-minute period is shown in Figure 1. Dips in saturation were accompanied by increases in heart rate of 10–40 beats per minute. The patient's mean saturation overnight was 93.8%. Thirty-three minutes (6.7% of the night) was spent at Sao_2 values below 90%, of which 14 minutes were spent below 85% Sao_2.

Intra-operative course

The patient underwent an uneventful repair of his aorto-duodenal fistula. Premedication was with lorazepam 3 mg. Anaesthesia was induced by thiopentone 100 mg and fentanyl 1 mg. Intubation of the trachea was performed following pancuronium 8 mg. Maintenance of anaesthesia was with isoflurane and 30% oxygen in nitrous oxide, and the operation lasted 3 hours. The patient's lungs were ventilated after operation in the ITU for 4 hours and he received 2 mg of intravenous morphine during this period.

Postoperative course

Computer-assisted monitoring and direct observation of the patient commenced 4 hours after tracheal extubation (8 hours after the end of the operation). In the first 4 hours after extubation we observed 246 episodes of abnormal respiratory pattern lasting 10 seconds or longer. Table 1 shows the patterns of respiration that were observed and the mean duration of the events. During this period the patient breathed 50% oxygen via a facemask. These events resulted in only three episodes of desaturation to < 85% because of the supplementary oxygen.

The majority of the respiratory events were purely obstructive. Many (labelled 'mixed' in Table 1) began with an initial central apnoea indicated by zero airflow and absent oesophageal pressure changes, followed by an obstructed pattern with respiratory effort increasing progressively (pressure changes become increasingly negative and there was no airflow). We saw paradoxical thoraco-abdominal movements. Ventilatory 'breakthrough' and a hypernoeic respiratory pattern would then occur, often associated with an arousal during which the patient appeared very distressed. The patient would then rapidly return to sleep; the cycles repeated. His distress with each arousal was interpreted as pain, and he was prescribed a further 7 mg of morphine in 1-mg intravenous boluses over the 4 hours, despite his severe drowsiness and rapid sleep onset.

Use of nasal CPAP

Nasal CPAP (5 cmH_2O) was administered after 4 hours of observation. The patient fell asleep within 5 minutes and remained asleep for 8 hours with no further episodes of respiratory obstruction.

Figure 2 shows an example of the pattern of the blood pressure changes associated with episodes of respiratory obstruction prior to administration of nasal CPAP. Data points were plotted for systolic blood pressure beat-to-beat with a computer-generated line drawn between successive points. The large breath-to-breath fluctuations in blood pressure in the troughs marked A are the result of major intrathoracic pressure swings attributed to the increased respiratory effort during obstructive apnoea (pulsus para-

Table 1. Respiratory study on the first postoperative night (ITU).

Type	Number of events	Mean duration (seconds)	Range (seconds)
Obstructive	134	19.3	11–30
Mixed	104	20.5	10–33
Central apnoea	8	14.6	10–21
Number of respiratory events (> 10 seconds) in 4 hours = 246.			

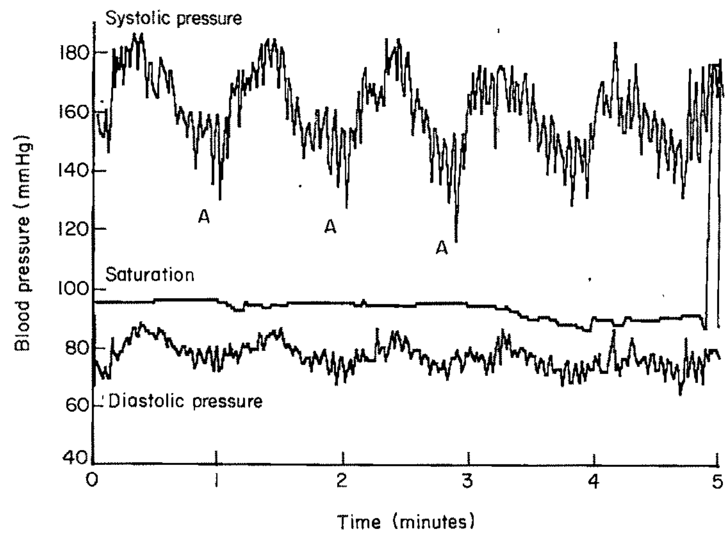

Fig. 2. Postoperative blood pressure fluctuations observed during obstructed breathing. Tracings show systolic and diastolic blood pressure during obstructed breathing. Large pulsus paradoxus in troughs marked A are the result of negative intrapleural pressure swings consequent upon obstruction. Peaks of blood pressure with smaller pulsus paradoxus coincide with arousal, release of obstruction and hyperpnoea.

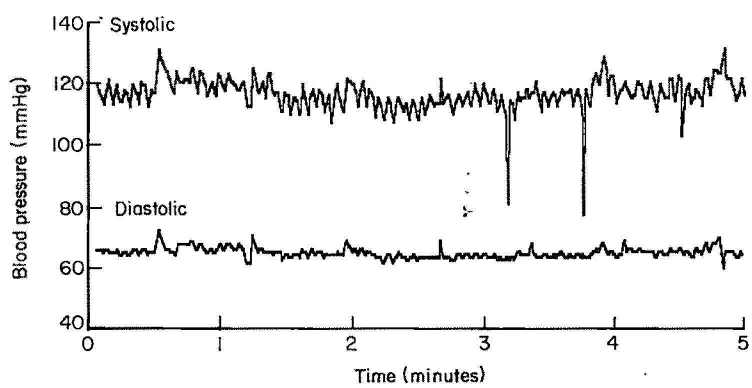

Fig. 3. Postoperative blood pressure fluctuations following nasal CPAP. Large peaks in blood pressure were abolished following relief of respiratory obstructions using nasal CPAP.

doxus). The sudden increase in systolic blood pressure following the troughs coincided with an arousal and release of the obstruction. During the hyperpnoea following release of the obstruction, large negative intrathoracic pressures were developed during inspiration and a pulsus paradoxus superimposed on the raised blood pressure. After a short period of unobstructed respiration, blood pressure fell; and then the cycle would repeat. Heart rate changes with the obstructions were present but were less than the changes before operation. Oxygen saturation changed relatively little, (FiO_2 0.50).

Figure 3 shows blood pressure following the start of nasal CPAP, and is representative of the rest of the night. The cyclic rises in blood pressure to hypertensive levels have disappeared. The transducer position for the Finapres was at the same level relative to the heart in both Figures 2 and 3. Table 2 shows blood pressure data for similar periods before and after treatment with nasal CPAP. The reductions in mean systolic, diastolic and mean blood pressure after CPAP were 27.7%, 16%, and 25% respectively.

Subsequent postoperative course

The patient was transferred to the ward on the second postoperative day and remained free of CPAP.

Table 2. Blood pressure during obstructed breathing and following treatment with Nasal CPAP. Data are expressed as mean and (SD).

	Obstructed breathing	Nasal CPAP
Number of heart beats analysed	995	990
Systolic; mmHg	154.2 (14.5)	112.2 (5.2)
Diastolic; mmHg	75.3 (5.7)	63.3 (2.4)
Mean BP; mmHg	95.1 (7.4)	76.4 (2.9)

Supplementary oxygen was discontinued after the second night postoperatively. Episodic dips in Sa_{O_2} returned on the 5th to the 9th postoperative nights, and mean Sa_{O_2} remained below the pre-operative level.

Discussion

Obstructive sleep apnoea is characterised by episodes of upper airway obstruction which result in a disruption of sleep and hypoxaemia.[3] Normally the upper airway muscles increase their tone in inspiration and keep the pharynx open against the subatmospheric pressure generated by inspiratory flow. Anatomical factors which narrow the upper airway necessitate an increased subatmospheric pressure in the pharynx during inspiration, and may render muscular splinting inadequate. As a consequence the pharynx may collapse on inspiration.

Obstructive apnoea is associated with periodic fluctuations in heart rate and blood pressure.[4–7] In the obstructed phase the increased respiratory effort generates a more negative intrapleural pressure. This is transmitted to the mediastinal structures and causes a fall in blood pressure and an increase in transmural pressure across the heart and great vessels. The increased transmural pressure increases left ventricular afterload.[8,9] There may also be further hydrostatic effects with pooling of blood in the lungs and an increase in venous return to the right heart which produces a shift of the interventricular septum to the left, and impedes filling of the left ventricle.[10] Tachycardia develops, presumably due to a sympathetic response to the hypotension, arousal, hypoxaemia, and hypercarbia.

The patient in this report had a history of snoring and was overweight, especially around the neck, and required a 17 inch collar. It has been suggested that the best predictor of those at risk from obstructive sleep apnoea is a neck circumference > 110% of predicted.[11] However, he gave no history of poor sleep or excessive daytime sleepiness. Pre-operative nocturnal oximetry demonstrated severe episodic desaturation. Such overnight pulse oximetry may be useful before operation to identify patients who snore heavily and are at risk from postoperative obstructive apnoea. Such monitoring needs to have good resolution as events may not last much longer than 10 seconds.

Postoperative respiratory obstructions were associated with large fluctuations in systolic and diastolic blood pressure in this patient, as has been observed in nonsurgical patients with obstructive sleep apnoea.[4–7] Repeated increases in blood pressure and heart rate (especially if accompanied by decreases in Sa_{O_2}) may be harmful to patients with ischaemic heart disease. Such pressure changes are undesirable after aneurysm repair. Nasal CPAP prevented respiratory obstruction and there was a lower and more stable blood pressure. There were fewer interruptions of sleep after starting nasal CPAP. No opioid was required in the next 8 hours.

Nasal CPAP is an effective treatment for obstructive sleep apnoea[12] and patients who present for surgery with this condition who are already on nasal CPAP should resume the treatment as early as possible in the post-operative period. Previously undiagnosed patients who have obstructive sleep apnoea after operation should be considered promptly for treatment with nasal CPAP in the postoperative period. A nasopharyngeal airway may prove to be a successful alternative in some patients.

In spite of moderately severe obstructive sleep apnoea after operation and immediately following extubation, this patient did not have severe respiratory obstruction when nasal CPAP was discontinued upon discharge from ITU 24 hours after surgery. It was not until the fifth postoperative night that a large number of desaturations recurred (as a result of which he spent 6% (30 minutes) at less than 85% saturation). The relative absence of dips during nights 3 and 4 may be related to the patient's lack of sleep, or the pattern of sleep obtained. Electroencephalographic studies after abdominal surgery have shown slow wave and rapid eye movement (REM) sleep to be almost completely abolished for the first 2–3 days after surgery. A rebound in the amount of REM sleep occurred on night 5.[13] Because obstructive sleep apnoea is increased in incidence and severity in REM sleep, it may be speculated that its reappearance in our patient reflects increased REM sleep. The importance of these late postoperative desaturations and the accompanying heart rate and blood pressure fluctuations, as adverse factors in a patient's recovery, remains to be determined. Reduction in wound oxygen tension is known to reduce wound healing and promote infection[14,15] and recently it has been shown that pulmonary oxygenation is the main determinant of the partial pressure of oxygen subcutaneously in surgical wounds following abdominal surgery.[16] Our patient developed a severe wound infection and dehiscence which required several weeks extra admission and may have contributed to a re-infection of his aortic graft, a recurrence of his aortoduodenal fistula, and ultimately, death from exsanguination 7 months after surgery.

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Anaesthesia, 1991, Volume 46, pages 854–857

CASE REPORT

Acute airway obstruction as a result of minitracheotomy

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Summary

We describe two cases of airway obstruction due to bleeding following minitracheotomy and discuss the indications for minitracheotomy and management of this complication.

Key words

Equipment; minitracheotomy.
Complications; airway obstruction.

Percutaneous minitracheotomy has an established role in the management of sputum retention.[1] The technique is not without risk; the main complications are haemorrhage,[2,3] surgical emphysema,[4,5] misplacement[6,7] and displacement.[8,9] We describe two cases where haemorrhage into the trachea, with rapid thrombus formation, produced life threatening respiratory obstruction not relieved by tracheal intubation.

Case history 1

A 55-year-old man with Guillain–Barré syndrome was admitted to the intensive care unit in respiratory failure. After 3 days of artificial ventilation of the lungs his condition had improved sufficiently to allow tracheal extubation. Because of subsequent sputum retention a minitracheotomy was performed.

Bleeding from the site of the minitracheotomy, which had initially been insignificant, increased in volume over the next hour despite apparently normal coagulation. He developed respiratory obstruction with cyanosis which did not respond to 100% oxygen by facemask. His trachea was intubated following etomidate 8 mg and suxamethonium 100 mg. Manual ventilation of the lungs proved to be impossible, but on deflation of the tracheal tube cuff ventilation became possible and the oxygen saturation rose. The trachea was re-intubated with a different tracheal tube. Again, inflation of the lungs was impossible until the tube cuff was deflated.

Rigid bronchoscopy revealed a clot which partially occluded the trachea, particularly in expiration. It was not possible to remove this through the bronchoscope, so a formal tracheostomy was performed, which enabled the removal of the clot. This was a cylindrical cast 11 cm × 5 cm that on histological examination proved to consist solely of organised thrombus. The tracheostomy was successfully closed two weeks later, and subsequent recovery was uneventful.

Case history 2

A 61-year-old woman underwent a left thoracotomy and oesophagogastrectomy for carcinoma of the oesophagus. The immediate postoperative period was complicated by fluid overload and pneumonia that required treatment by intermittent positive pressure ventilation for 9 days. Her trachea was then extubated.

By the 11th postoperative day sputum retention was diagnosed. A minitracheotomy was performed easily under local anaesthesia but some bleeding occurred. Coagulation studies that day were normal. The minitracheotomy cannula was aspirated at frequent intervals, which yielded moderate amounts of blood and secretions. One hour following the minitracheotomy, the patient became cyanosed, with signs of upper airway obstruction. Manual ventilation of the lungs with 100% oxygen via a facemask was impossible and the trachea was intubated following intravenous etomidate 8 mg and atracurium 30 mg. There was complete obstruction to air entry and the tracheal tube was removed. Laryngoscopy revealed material lying between the vocal cords, which when removed using Magill's forceps, proved to be an organised thrombus measuring 2 cm by 9 cm. The trachea was immediately re-intubated and the lungs inflated easily. A formal trache-

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ostomy was performed to achieve haemostasis. The patient ultimately made a good recovery, and was discharged home 4 weeks after operation.

Discussion

Since the introduction of minitracheotomy in 1983, the technique has played an important role in the management of respiratory problems, particularly sputum retention.[1,10] Minitracheotomy has also been used to provide access to the trachea for emergency ventilation,[11] and in the treatment of respiratory failure with a high frequency jet ventilator.[12]

External bleeding from skin and subcutaneous tissues is common following insertion of the minitracheotomy cannula. It may be minimised by the use of a local anaesthetic containing a vasoconstrictor.[10] Terry and Cook,[3] described a method of reducing haemorrhage following minitracheotomy by alteration of the incision. In both of our cases early bleeding occurred into the airway, with rapid formation of thrombus and respiratory obstruction, despite normal coagulation in both cases. A recent example of severe haemorrhage occurred in a patient with a subglottic polyp who was taking anticoagulants.[2] There was no evidence of subglottic granuloma in either of the cases described.

In one of our patients, tracheal intubation failed to relieve the airway obstruction and mimicked the obstruction produced by tracheal cuff herniation. We do not believe this to be the cause here, since the problem was not corrected by changing the tracheal tube. It is possible that inflation of the cuff may have diverted the open end of the tube into the thrombus. In the second case, it was fortunate that the thrombus was visible in the glottis and easily removed. It had not been observed during first laryngoscopy. Removal of the tracheal tube resulted perhaps in the clot being displaced to the level of the glottis. In both cases the minitracheostomy was performed by an experienced surgeon on an intensive care unit. Had the ensuing events occurred on a general ward, personnel skilled in airway management, and bronchoscopy equipment, may not have been readily available, with potentially fatal results.

It is fortunate that in neither case did the patients suffer from the consequent hypoxia. We recommend that minitracheotomy should only be carried out in an operating theatre or the intensive care unit where facilities for resuscitation and rapid and difficult intubation are immediately available. Awareness of this complication of internal bleeding and thrombus formation may help in early diagnosis and prompt treatment of respiratory obstruction following minitracheotomy.

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CASE REPORT

Marked decrease in arterial oxygen tension associated with continuous intravenous nifedipine administration

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Summary

Intravenous nifedipine was administered to treat arterial hypertension in a 54-year-old woman presenting for removal of a meningioma. A marked decrease in arterial oxygen tension occurred during the nifedipine infusion. Inhibition of hypoxic pulmonary vasoconstriction by nifedipine is discussed.

Key words

Pharmacology; calcium channel blockers, nifedipine
Lung; hypoxic pulmonary vasoconstriction.

Nifedipine, a potent calcium entry blocker and systemic vasodilator, has been used to treat angina pectoris, hypertension, and myocardial infarction. While many vasodilators have been found to inhibit hypoxic pulmonary vasoconstriction (HPV),[1–3] the effects of intravenous nifedipine on HPV are reported to be variable.[4–6] We describe a neurosurgical patient who experienced a precipitous decrease in Pa_{O_2} during an intravenous nifedipine infusion.

Case history

A 54-year-old, 62-kg, 167-cm woman presented for removal of a left frontal meningioma. Her past medical history was unremarkable except for arterial hypertension which was treated with oral nifedipine 10 mg three times daily. On the pre-operative visit, no abnormalities of the cardiovascular and pulmonary system were found. The blood pressure was 125/80 mmHg and the ECG showed a normal sinus rhythm at a rate of 78 beats per minute. Physical examination of the lungs and a posterior–anterior chest X ray were unremarkable. All pre-operative laboratory data were within normal limits. Arterial blood gas (ABG) analysis showed a pH 7.41, Pa_{O_2} 9.6 kPa, and Pa_{CO_2} 5.1 kPa whilst breathing room air. Dexamethasone 8 mg was given intravenously the day before operation.

On the day of operation, the patient received nifedipine 10 mg orally 90 minutes and midazolam 5 mg intramuscularly 20 minutes before arriving in the operating room. Blood pressure was 160/90 mmHg and heart rate 92/minute. Anaesthesia was induced with midazolam 10 mg, fentanyl 0.5 mg, and pancuronium 6 mg intravenously. The trachea was intubated, and ventilation was controlled with nitrous oxide 50% and oxygen 50%. With induction of anaesthesia, the blood pressure decreased to 140/80 mmHg, and the heart rate remained essentially unchanged. General anaesthesia and paralysis were maintained with fentanyl, midazolam, 50% nitrous oxide in oxygen, and pancuronium. Intra-operative monitoring included arterial blood pressure measurement, central venous pressure (CVP) measurement, pulse oximetry, capnography, and measurement of the $F_{I_{O_2}}$.

The patient was placed in the supine position in a Mayfield fixation apparatus without change in monitored variables. An initial ABG sample, 35 minutes after induction of anaesthesia at an $F_{I_{O_2}}$ of 0.5, showed a pH of 7.48, a Pa_{O_2} of 37.8 kPa, and Pa_{CO_2} of 3.9 kPa. The peripheral oxygen saturation (Sp_{O_2}) was 99%. The surgical incision was made 50 minutes after induction of anaesthesia (B on Fig. 1). Despite incremental doses of fentanyl, midazolam, and droperidol the blood pressure slowly increased to 180/110 mmHg. There was no alteration in heart rate, and end-tidal CO_2 remained at 3.3 vol%. Volatile anaesthetic agents were not added. A bolus of nifedipine (Adalat, Bayer Leverkusen) 1 mg intravenously, followed by a continuous infusion of 0.3 μg/kg/minute was given. The blood pressure decreased to 130/75 mmHg within 5 minutes. There was a gradual decrease in Sp_{O_2} from 99 to 95% during the 45 minutes after the beginning of the nifedipine infusion. An ABG revealed that the Pa_{O_2} had decreased to 11.3 kPa at an $F_{I_{O_2}}$ of 0.5. The $F_{I_{O_2}}$ was changed to 1.0,

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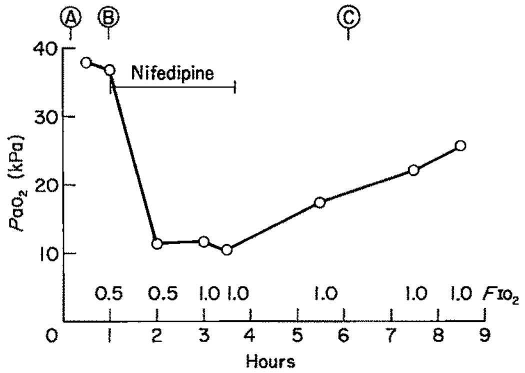

Fig. 1. Measured Pa_{O_2} values at F_{IO_2} 0.5 or 1.0. The time of nifedipine administration is marked. Point A represents induction of anaesthesia, B surgical incision, and C end of surgery.

with Sp_{O_2} remaining at 95%. There were no changes in ECG, blood pressure, or airway pressure during this period. Breath sounds were equal on each side. Flexible bronchoscopy showed the tip of the tracheal tube 3 cm above the carina, and all bronchial ostia patent. The haemoglobin was 12.4 g/dlitre, and the CVP was unchanged at 7 mmHg. After 2 hours 45 minutes of nifedipine infusion, the Pa_{O_2} was 10.4 kPa at an F_{IO_2} of 1.0. Nifedipine was discontinued, and the Pa_{O_2} slowly increased over several hours (Fig. 1).

Discussion

Changes in Pa_{O_2} are common during anaesthesia. In our patient, Pa_{O_2} decreased during operation from 37.8 kPa at F_{IO_2} 0.5 to 10.4 kPa at F_{IO_2} 1.0. Auscultation, bronchoscopy, and the postoperative chest X ray showed no incorrect position of the tracheal tube, no aspiration, progressive atelectasis, pneumothorax, or pulmonary oedema; fat and pulmonary embolisms seemed very unlikely. Thus, inhibition of HPV by nifedipine is a likely explanation for the decrease in Pa_{O_2} in our patient.

HPV diverts blood flow away from hypoxic regions to better ventilated areas of the lung[7] and general anaesthetics modify this effect.[8-10] Intravenous anaesthesia based on a narcotic technique is said to have only minimal influence on HPV.[11] Many other factors influence the HPV response such as alterations in pulmonary artery and pulmonary venous pressures, alveolar P_{O_2}, mixed venous oxygen tension, and cardiac output.

Cardiovascular agents are known to inhibit HPV. Nitroglycerin is a predominant venodilator, and sodium nitroprusside is a predominant arteriolar dilator.[1-3,12-15] Cardiac output increased by positive inotropic agents may also influence intrapulmonary shunting.[16-17] The change in cardiac output induced by the nifedipine infusion would not explain the precipitous decrease in Pa_{O_2} seen in our patient. There were no signs of increased intracranial pressure which could have caused secondary cardiovascular changes.[18]

Nifedipine is widely used in the treatment of hypertension. Since the intra-operative hypertension was unresponsive to fentanyl, midazolam, and droperidol, a continuous intravenous nifedipine infusion was started, which decreased the blood pressure to 130/75 mmHg. Nifedipine is a potent dilator of resistance vessels.[19] Kennedy *et al.* demonstrated that nifedipine is a potent pulmonary vasodilator and may inhibit HPV.[6] In acute respiratory failure, nifedipine inhibits HPV without reducing arterial oxygen saturation or delivery.[20] From a study in mongrel dogs Casthley *et al.* concluded that nifedipine infusion significantly alters oxygenation.[4] Boldt *et al.* demonstrated in cardiac patients with normal lung function that intravenous nifedipine dilated pulmonary vessels and increased cardiac output without increasing intrapulmonary shunting.[5] Our patient had no pulmonary dysfunction, nevertheless, arterial oxygen tension decreased markedly during intravenous nifedipine infusion. The slow recovery of arterial oxygenation after stopping nifedipine in our case is compatible with an elimination half-life of 4–5 hours.[21]

In summary, inhibition of HPV by intravenous nifedipine may even affect patients with normal pulmonary function.

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CASE REPORT

Exaggerated epidural blockade resulting from unusual spread of bupivacaine in a patient with low back pain

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Summary

A 75-year-old woman with chronic low back pain was given bupivacaine and methylprednisolone epidurally through a catheter in the L_1–L_2 interspace. An unusual spread of bupivacaine resulted in a block from the C_4 to the L_1 dermatome with no relief of back pain. Injection of a radiopaque dye and subsequent X rays showed a similar spread. The possible causes are discussed.

Key words:

Anaesthetic techniques, regional; epidural.
Complications.

The injection of local anaesthetic and steroid by the epidural route has been recommended for the conservative management of back pain from nerve root compression[1] which may result from spinal stenosis. However, there are no reports of an exaggerated spread of epidural blockade in these patients. The patient had spinal stenosis as a result of spondylolisthesis and facet joint disease of the L_4–L_5 vertebra. An epidural injection of bupivacaine resulted in a bilateral block extending from the L_1 to the C_4 dermatomes.

Case history

A 75-year-old woman with exacerbation of chronic low back pain was admitted to the Pain Relief Unit. She had a 6-year history of low back pain which had become worse in the 6 weeks before admission with associated pain in the right leg. The back pain, which radiated to the back of the thigh and the outer aspects of the right leg and foot, was associated with tingling, numbness and weakness that resulted in difficulty in walking. Ibuprofen 600 mg 8 hourly, buprenorphine 0.4 mg 6 hourly, Tylex (codeine phosphate 30 mg, paracetamol 500 mg) two tablets 6 hourly, and prothiadine 50 mg at night provided no pain relief. A week before her admission, a single shot lumbar epidural injection of 0.5% plain bupivacaine 4 ml and methylprednisolone 80 mg gave her some pain relief but the extent of the block was not recorded. An X ray of the lumbar spine at her initial visit 6 years earlier had shown a spondylolisthesis of L_4 on L_5 vertebra. She was 155 cm tall and weighed 80.1 kg. The cranial nerves were intact. Power on dorsiflexion and planter extension was reduced in the right foot. Tone was normal in all limbs and there was loss of sensation to pinprick over a wide area in the right leg covering dermatomes L_2–L_5. All the reflexes were present and the planter responses were downgoing. Straight leg raising was 60 degrees on the right and 80 degrees on the left side. All the movements of the back were limited by pain. A decision was made to admit her for a trial of epidural local anaesthetic and steroids while awaiting myelography and consultation with the neurosurgeons.

Procedure

A 16-gauge epidural needle was inserted at the L_1–L_2 interspace with the bevel facing caudally and a catheter threaded so that 4 cm was left inside the epidural space. After negative aspiration for CSF and blood, 0.5% plain bupivacaine 3 ml and methylprednisolone 80 mg were injected. The patient had no relief of pain and there was no demonstrable sensory or motor blockade. A further 10 ml of 0.5% plain bupivacaine was injected after about one hour over a period of one minute with the patient supine. The pulse rate, arterial pressure and respiratory rate were monitored every 5 minutes. After 15 minutes, the patient complained of feeling faint and her arterial pressure had fallen to 74/50 mmHg from a pre-injection level of 130/80 mmHg. She still complained of pain. There was loss of pinprick sensation from C_4 down to T_{12}–L_1 dermatomes bilaterally and power was normal in the lower limbs. She

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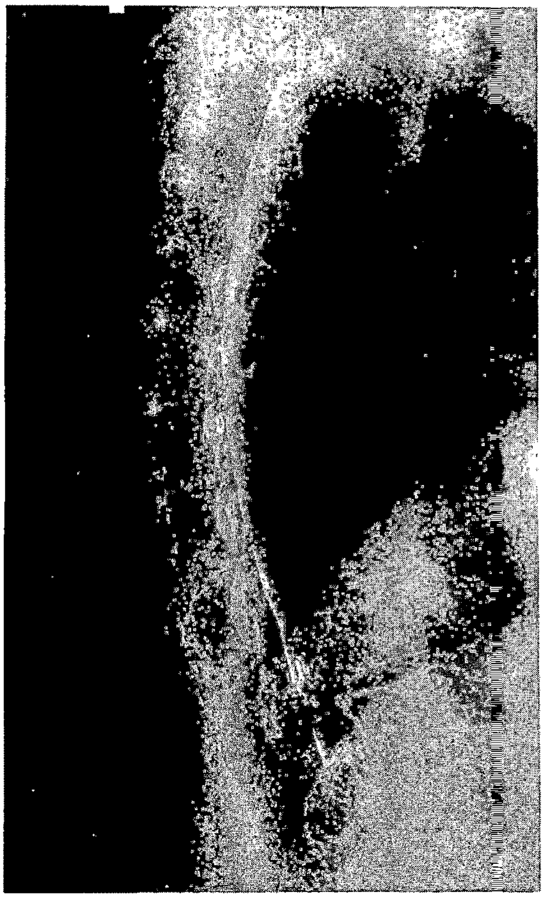

Fig. 1. Spread of 1.2 ml radiopaque dye extending to upper thoracic segments (total injected volume 1.5 ml, catheter dead space 0.3 ml).

was given intravenous fluids and ephedrine 9 mg in 3-mg increments. She felt better and the arterial pressure rose to 120/70 mmHg. Observations were continued regularly. The maximum caudal spread was to the L_1 dermatomes and approximately 2 hours after the injection of bupivacaine there was no detectable block.

Twenty-four hours later, 1 ml of a radiopaque dye (Niopam) was injected into the epidural catheter. An X ray of the spine showed dye in the subcutaneous tissue and on inspection it was clear that the catheter had been displaced from the epidural space. To establish the nature of the unusual spread of bupivacaine, it was decided to repeat the epidural injection. An epidural catheter was satisfactorily inserted in the T_{11}–T_{12} interspace and 1.5 ml of radiopaque dye injected. An X ray of the spine showed the dye spreading to the upper thoracic segments but the caudal spread was restricted to the L_1–L_2 as seen in Figure 1. Two days later, a myelogram was performed which revealed a spinal stenosis due to grade 1 spondylolisthesis of L_4 on L_5 vertebra and facet joint degeneration. The patient had a decompressive laminectomy at L_4–L_5 following which she had complete relief of pain in the right leg but continued to have some back pain when seen in the pain clinic 2 months after the operation.

Discussion

In this patient, injection of 0.5% plain bupivacaine 10 ml into the epidural space at L_1–L_2 interspace resulted in two unusual observations. First, the cephalad spread was exaggerated and reached the C_4 dermatome, and second, the caudal spread was restricted at the L_1 dermatome. The extent to which local anaesthetic solutions spread in the epidural space depends on several factors including site of injection, age and height of the patient and dose of local anaesthetic (volume × concentration).[2] The block is quicker and intense in the region of the injection. A gradual reduction in dosage is necessary to produce blockade of the same number of dermatomes from ages 20–80 years.[3] Sharrock[4] has also shown high levels of blockade in aged patients regardless of dose. Increasing doses are required with increasing height. Our patient was 75 years old and 155 cm tall and we were aware of the reduced dose requirements. A total of 16 segments were blocked bilaterally (12 thoracic and four cervical), giving a dose of 0.6 ml/segment; this is less than the recommended volume per segment.[2]

Causes of an exaggerated spread of local anaesthetic include accidental subarachnoid and subdural injection. Patients with arteriosclerosis and diabetes mellitus require smaller doses and may present with exaggerated blocks when given normal doses.[5] These conditions were not present in our patient. A subarachnoid injection was unlikely for several reasons. No CSF was aspirated and the initial 3 ml of bupivacaine did not produce any block. Furthermore, 10 ml of bupivacaine 0.5% injected intrathecally would have caused a massive block with resultant loss of consciousness and apnoea and the events would have occurred much quicker. Subdural injection of local anaesthetic usually results in bizarre spread resulting in a patchy and assymetrical block.[6] When contrast media are injected into catheters in the subdural space, they do not move freely and cause a sausage-shaped shadow as a result of the material travelling up and down the thecal tube. Although we had to remove our first catheter and inject the dye through a second one, the spread of the dye was similar to the spread of bupivacaine seen with the first catheter, and radiologically the second catheter was shown to be in the epidural space. Hence it is unlikely that the first catheter was in the subdural space.

The symptoms and signs of nerve root compression and demonstration of spondylolisthesis at L_4–L_5 on X ray indicated the level of the disease. Burn *et al.*[7] in a study using epidurograms in patients with lumbosciatic syndromes have shown that an injection of 20 ml of a mixture of local anaesthetic, steroid and dye via the lumbar route spreads cephalad to the low dorsal segments, but in half the patients there is no spread below L_5. In our patient the block did not spread caudally beyond the L_1 dermatome and this was confirmed on X ray by injecting a radiopaque dye. We believe that the obstruction to the free flow of fluid in the epidural space was not the result of the disease process at L_4–L_5, which was causing the pain and other symptoms and signs, but was at a higher level of L_1 and causing no symptoms or signs. It is possible that the block reached the cervical segments because of an obstruction at the L_1 level. The obstruction to free flow of fluid in the epidural space at the L_1 level may have resulted from several causes. It may be due to age-related osteoarthritic changes, resulting in a narrowing of the bony canal and limitation of the epidural space, or the result of the previous epidural injection, performed one week earlier. This could have produced an epidural haematoma, without any symptoms or signs, but preventing the normal spread

of local anaesthetic. A combination of the above factors may have been responsible. Whatever the source of the obstruction, it did not cause any symptoms or signs. We recommend that in older patients in the circumstances we have described, small incremental doses of local anaesthetic solutions be used and their effects carefully monitored.

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Anaesthesia, 1991, Volume 46, pages 862–863

CASE REPORT

Paraplegia following coeliac plexus block

R. T. M. VAN DONGEN AND B. J. P. CRUL

Summary

A case is described in which a coeliac plexus block with alcohol 48%, performed under X ray control, resulted in paraplegia. Ischaemia of the spinal cord, due to damage to the arterial blood supply, was thought to be the cause.

Key words

Anaesthetic techniques, regional; coeliac plexus block.
Complications; paraplegia.

Coeliac plexus block involves injection of a neurolytic agent close to the spinal cord.[1] It is remarkable, therefore, that severe neurological complications after coeliac plexus block are rarely reported.[2–5] Until 1989, paraplegia had only been described in the literature on three occasions.[2–4] The technique had been performed correctly in each case, therefore damage to the blood supply of the spinal cord was thought to have been the cause. We describe a patient in whom a coeliac plexus block using alcohol 48%, performed under radiographic control, resulted in paraplegia.

Case history

A 66-year-old man had undergone partial left colectomy for obstructive adenocarcinoma of the colon 2 years previously. There was local penetration of the serosa and regional lymph node spread and the tumour was classified as Duke's stage IV. A year later, during laparotomy for peritonitis as a result of rupture of a hepatic cyst, metastases were found in the liver, mesentery and retroperitoneal/paraaortic lymph nodes. In the following months, chemotherapy with 5-fluorouracil (5-FU) was started, but this had to be discontinued because of dyspnoea, which was thought to be because of cardiac failure secondary to cardiotoxic effects of the 5-FU.

Ten months after the second laparotomy, the patient complained of three different types of pain; pain in the right upper abdomen, possibly the result of liver metastases, pain high in the thoracic vertebral column without neurological symptoms and pain in the lower left abdominal quadrant related to defaecation.

The only abnormality shown on X ray was a decrease in the height of the fourth thoracic vertebra. There were no signs of vertebral dislocation or metastases. The upper abdominal pain was not relieved by acetaminophen, diclofenac, naproxen, buprenorphine and morphine sulphate 'slow-release' tablets, therefore a neurolytic coeliac plexus block was undertaken.[4,5]

The general condition of the patient was poor and he was unable to lie in the prone position for more than a few minutes. In view of this, the decision was made to omit a test dose of local analgesic before injecting the neurolytic agent.

The technique described by Moore[1] was used with the patient in the prone position. The procedure was performed under local analgesia but sedation was administered during injection of the alcohol.

Interpretation of the X rays was difficult because the patient was restless as a result of pain in his vertebral column.

The final positioning of the needle tips, 1–1.5 cm anterior to the ventral border of the first lumbar vertebra, was obtained and considered satisfactory from a radiological point of view.

Iohexol (omnipaque 300) was injected, and anteroposterior and lateral radiographic views confirmed good prevertebral vertical spread of the solution without signs of retrograde, epidural, intrathecal or intravascular spread.

The patient was sedated with etomidate 10 mg and after a negative aspiration test, lignocaine 1% 10 ml mixed with alcohol 96% 10 ml was injected through each needle. A decrease in blood pressure to 80/60 mmHg was treated with intravenous fluid administration (500 ml glucose 3.3%, saline 0.25%). Immediately after the procedure, the patient

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was transferred to the recovery room, and he awoke about 15 minutes later. Paralysis of the patient's legs was noted by the nurse at this stage but it was ascribed to the use of local analgesic.

Two hours after the procedure, complete paralysis and arreflexia of both legs, with loss of sensation below L_1, were present. There was slight movement in the hallux of the left foot but no movement at 12 hours. Oral dexamethasone (4 mg) was started immediately and prescribed four times daily.

Further neurological assessment, tomography of the vertebral column and magnetic resonance imaging showed no pathological fractures, compression of the spinal cord, or other reasons for his paraplegia. The patient died a month later, pain free, at home. The immediate causes for death were septic complications from a large pressure sore in the sacral region and pneumonia. Autopsy was not performed.

Discussion

Coeliac plexus block with a neurolytic agent is a possible treatment for upper abdominal pain due to cancer.[1,5] However, the indications for its use must be very strict,[6] since neurological complications are unacceptable in benign pain syndromes.

The use of radiographic control during the blockade, to increase the accuracy and reduce complications, is considered to be mandatory.[5] However, according to Thompson,[7] the use of X rays will not always prevent neurological complications since these can occur secondary to a vascular lesion of the spinal cord.[2–4]

In this case, the fact that the block did not go higher than L_1, suggests that the injection was not intrathecal. The rapid development of a symmetrical and complete neurological deficit below the puncture site, despite correct positioning of the needle tips and a normal spread of contrast medium, suggests a compromised blood supply to the spinal cord. In addition, the time course of events after injection and the absence of blood during aspiration, is suggestive of spasm or compression of a spinal artery, rather than intra-arterial injection.

Compression of the blood vessels within the confined retroperitoneal space could have possibly occurred, and in this patient a number of factors might have contributed to this. These include the presence of enlarged retroperitoneal lymph nodes, the poor general condition of the patient (e.g. cachexia, atrial fibrillation, hypotension) and the injection of a relatively large volume of fluid into the retroperitoneal space. The use of a test block with a local analgesic may not have prevented this complication since alcohol itself can cause vasospasm at a concentration of 96%.[6] In this case alcohol 48% was used and this might have contributed to the damage to the blood supply of the spinal cord.

The use of computerised axial tomography during injection may increase the success rate of the procedure and reduce the volume of neurolytic solution required,[1,8] but whether or not it decreases the complication rate is unknown. It is possible that the use of phenol, which causes less pain than alcohol, may avoid the need for sedation, thus allowing immediate detection of any neurological deficit during injection.[2]

In view of the variability of the arterial blood supply of the spinal cord, prevention of this severe complication cannot be guaranteed.[9] Therefore, in addition to the strict indications and precautions recommended by Bowen-Wright,[6] we suggest the following refinements to the technique. The position of the needles should first be confirmed radiologically using a small amount of the contrast medium (0.5–1 ml). A mixture of neurolytic agent and contrast medium (5 ml per 20 ml of neurolytic agent) should be injected slowly (20 ml/minute). The use of an extension tube connected to the needle prevents inadvertent movement during injection and unnecessary exposure of the operator's hands to radiation. Immediate control of spread of the fluid is possible with this technique. If sedation or general anaesthesia is inadvisable, epidural analgesia with bupivacaine 0.25% or prilocaine 1% may be used. This allows the patient to be positioned prone, but does not produce motor blockade in the lower limbs. In our experience of six patients, a volume of 8–12 ml administered at the L_1–L_2 interspace caused no motor blockade and allowed neurological evaluation during the procedure. While this paper was in preparation, we were made aware of another case similar to our own. In view of these cases, the critical remarks made by Sharfman and Walsh[10] and the good results from spinal opioid administration reported in these patients, we are becoming more reluctant to perform coeliac plexus blocks. In our opinion, there is need for a reassessment of the technique, its indications and side effects.

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CASE REPORT

Prolonged action of enoximone in renal failure

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Summary

Enoximone was administered on two separate occasions to a 37-year-old woman with renal failure secondary to thrombotic thrombocytopenic purpura. Plasma concentrations of enoximone and its principal metabolite, enoximone sulphoxide, were measured over a 9-day period. As renal function improved the rate of elimination of enoximone sulphoxide increased. The duration of effect of enoximone may be prolonged in patients with renal failure.

Key words

Phosphodiesterase inhibitors; metabolism.
Kidney failure; acute.

Enoximone is a selective phosphodiesterase inhibitor with inotropic and vasodilator properties. We describe a patient with changing renal function who received enoximone on two occasions, and in whom plasma concentrations of enoximone and its principal metabolite, enoximone sulphoxide, were measured.

Case history

A 37-year-old woman was admitted to the intensive care unit with a provisional diagnosis of postpartum thrombotic thrombocytopenic purpura resulting in renal failure. Enoximone was given on two occasions to optimise her cardiac index in an attempt to maintain renal perfusion, and to reduce a high systemic vascular resistance (SVR) associated with systemic hypertension. On the first day after admission a loading dose of enoximone (7.5 mg) was given, followed by an infusion which was titrated in the range of 10–18 mg/hour to maintain a satisfactory blood pressure by reducing the SVR. The infusion was discontinued after 24 hours with no adverse effects. A second loading dose of 7.5 mg was given on the 5th day after admission for recurrent hypertension and an infusion of 10 mg/hour was continued for 24 hours. The effects of enoximone on cardiac index, SVR, oxygen consumption and delivery are shown in Table 1. The patient subsequently made a complete recovery with a normal platelet count, renal function and blood pressure.

Blood samples taken during the course of her admission were analysed for enoximone and its metabolite, enoximone sulphoxide, using high pressure liquid chromatography. The accuracy of this assay was 98.0% ± 2.4 (SD) recovery for enoximone and 97.3% ± 1.8 for enoximone sulphoxide (Merrell Dow Pharmaceuticals). These results and their relationship to creatinine clearance are shown in Figure 1.

Although the plasma concentrations of enoximone decreased rapidly once the infusion was discontinued, the elimination of enoximone sulphoxide was greatly prolonged. As renal function improved, the rate of elimination of enoximone sulphoxide increased, with resultant lower plasma concentrations during and after the second period of administration.

Table 1. The effects of enoximone infusion on haemodynamic variables over the first 24-hour period of administration.

Time (hours)	0	3	10	12	24
Dose of enoximone; mg/kg/hour	0	0.2	0.3	0.23	0.2
MAP; mmHg	136	114	90	75	81
CI; ml/minute/m^2	4.2	5.4	6.8	5.7	9.1
SVR; dynes/second/cm^5	1305	969	602	616	392
DIO_2; ml/minute/m^2	595	862	1089	916	1182
VIO_2; ml/minute/m^2	92	194	136	172	182

MAP, mean arterial blood pressure; CI, cardiac index; SVR, systemic vascular resistance; DIO_2, oxygen delivery index; VIO_2 oxygen consumption index.

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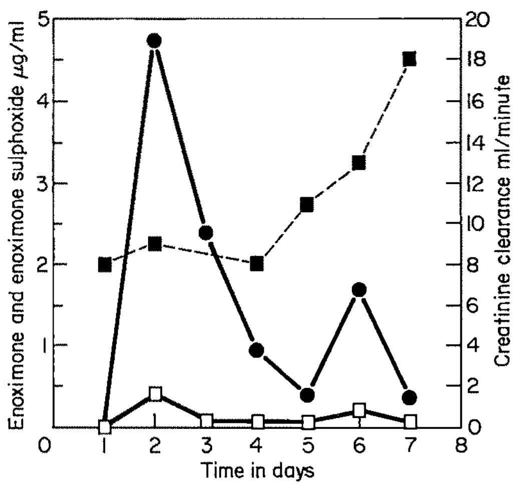

Fig. 1. Plasma concentrations of enoximone —□— and enoximone sulphoxide —●— in relation to creatinine clearance – – ■ – – during infusion of enoximone on days 1–2 and 5–6.

Discussion

Enoximone is metabolised mainly by oxidation to enoximone sulphoxide.[1] This is primarily excreted in the urine with only trace amounts as a sulphone or glycine conjugate. Enoximone sulphoxide shares the same inotropic and vasodilatory properties as the parent drug, but has only 14% of its potency. However, enoximone sulphoxide has a 13-fold longer duration of action and only 5% is bound to plasma proteins, as compared with 70% of enoximone. It is possible therefore that the metabolite may contribute to the pharmacodynamic action of enoximone, particularly in renal failure when the inability to eliminate enoximone sulphoxide may prolong its duration of action.

A complication related to the use of enoximone in a patient with renal impairment has already been described. Huggon and his colleagues[2] reported hyperosmolality related to the accumulation of propylene glycol in an infant treated with an infusion of enoximone.

In view of the delayed elimination of the metabolite seen in our patient we suggest that the duration of effect of enoximone may be prolonged in patients with renal failure. We would agree with Huggon and his colleagues[2] that the minimum effective dose should be used and if a continuous infusion of enoximone is needed in patients with renal failure then the dose should be closely monitored in view of the risk of accumulation of the active metabolite and the drug solvent.

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CASE REPORT

Life-saving use of extracorporeal membrane gas exchange in severe, acute respiratory failure

A. P. FISHER, B. JAYAWARDENE, K. D. RAMSTEAD AND A. R. FISHER

Summary

A 41-year-old man developed acute respiratory failure in association with thoracotomy and decortication for a persisting pleural collection secondary to a stab injury. The use of veno-venous extracorporeal membrane gas exchange proved life-saving.

Key words

Surgery; thoracic.
Complications; acute ventilatory failure.
Extracorporeal membrane oxygenation.

Case history

A 41-year-old Caucasian male was admitted to hospital complaining of malaise, shortness of breath and weight loss, having sustained a stab wound to the left chest one month previously. He had undergone exploratory thoracotomy in another hospital immediately after the assault and had been discharged after 9 days with residual haemothorax. He was readmitted there 3 weeks later with a large collection in the left pleural space. This was evacuated incompletely by insertion of a chest drain and the patient was referred to this hospital for thoracotomy and decortication.

On examination he was pale and dyspnoeic with the clinical and radiological signs of a left basal fluid collection and a purulent discharge via the chest drain.

The patient was given papaveretum and hyoscine preoperatively on the ward. Anaesthesia was induced with thiopentone, and a large, right, Robertshaw double-lumen tube was inserted after administration of suxamethonium. Anaesthesia was maintained by ventilation of the dependent right lung with nitrous oxide, oxygen and isoflurane. Muscle relaxation was achieved with atracurium and fentanyl was given to provide analgesia during the procedure. Monitoring included electrocardiography, continuous direct blood pressure (BP) measurement via a radial artery cannula and arterial oxygen saturation (Spo_2) with a pulse oximeter.

The findings at thoracotomy were a collection of blood clot and serosanguinous fluid, a left hemidiaphragmatic defect with adherent, prolapsing omentum and a healed laceration of the upper pole of the spleen, all of which appeared to have been caused by the original injury. Evacuation of clot and fluid, decortication and diaphragmatic repair were performed.

Surgery and anaesthesia proceeded uneventfully for 20 minutes with mild hypotension (systolic BP 80–100 mmHg) and Spo_2 > 95% on one-lung ventilation until, without significant blood loss, and for no apparent reason, the patient became profoundly hypotensive and hypoxic (Spo_2 60%). Inspired oxygen fraction (Fio_2) was increased to 1.0, correct position of the Robertshaw tube confirmed and continued, adequate ventilation of the dependent lung assured. Rapid infusion of one litre of Gelofusine restored the blood pressure but Spo_2 remained variably depressed at 80–90% despite the application of positive end-expiratory pressure (PEEP) to the lower lung and insufflation of the upper lung with oxygen. Ventilation of both lungs was resumed with Fio_2 0.6 and Spo_2 improved to 93%. The patient was haemodynamically stable but peripherally cool

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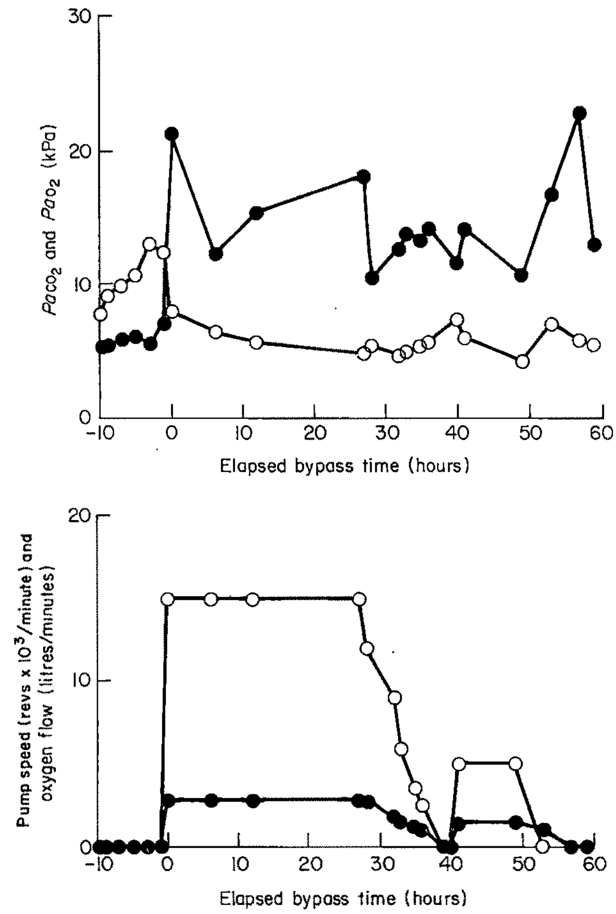

Fig. 1. Serial values of arterial oxygen (●) and carbon dioxide (○) tensions (upper panel), oxygen flow rate (○) and circuit pump speed (●) (lower panel) in a patient with severe, acute respiratory failure treated with extracorporeal membrane gas exchange. Time 0 represents institution of bypass.

at the end of the procedure; estimated blood loss was one litre and 2 units of blood were transfused.

A presumptive diagnosis was made of acute respiratory failure secondary to toxaemia provoked by operative disruption of the pleural collection. Treatment with cefuroxime, metronidazole and gentamicin was begun. No organism was isolated subsequently from specimens taken at the time of operation, but we believe that severe adult respiratory distress syndrome secondary to endotoxin release remains the most likely diagnosis.

The patient was transferred to the Intensive Care Unit (ICU) with worsening gas exchange.

Arterial carbon dioxide tension (Pa_{CO_2}) increased to 12.9 kPa, and arterial oxygen tension (Pa_{O_2}) could not be increased above 6 kPa despite a minute volume of 22 litres, FI_{O_2} 1.0 and PEEP of 10 cmH_2O. Peak airway pressure remained within normal limits at 20–30 cmH_2O. The patient became pyrexial and hypotensive, and inotropic support was required.

Extracorporeal membrane gas exchange was instituted 12 hours after operation. A veno-venous circuit (a Centrimed centrifugal pump connected in-line with a Scimed SM25 membrane oxygenator) was established from the right common femoral vein to the right internal jugular vein. The initial pump speed of 2800 rpm provided a bypass blood flow rate of 1.5–2.0 litres/minute. The oxygen flow rate through the oxygenator, initially 15 litres/minute, was adjusted to keep the Pa_{CO_2} at about 6 kPa. The activated clotting time (ACT) was maintained at about 300 seconds with a heparin infusion. The lungs were ventilated 'normally' at 10 litres per minute with an FI_{O_2} of 0.5 and PEEP of 5 cmH_2O during the period of veno-venous bypass.

There was an immediate improvement in the arterial blood gases following the institution of bypass and satisfactory values were maintained over the next 28 hours (Fig. 1). The pump speed and oxygen flow rate were then reduced gradually until support was withdrawn for one hour after 39 hours of bypass time. A simultaneous decrease in Pa_{O_2} and increase in Pa_{CO_2} at this time were reversed by reinstitution of bypass at a reduced level for a further 13-hour period, after which the extracorporeal circuit was withdrawn successfully.

Ventilator settings at cessation of extracorporeal support were minute volume 15 litres, FI_{O_2} 0.5 and PEEP 5 cmH_2O. The patient was weaned from the ventilator and his trachea extubated on the following day. He was discharged from ICU on the fourth postoperative day breathing 40% oxygen at atmospheric pressure; the Pa_{O_2} was 13.6 kPa and Pa_{CO_2} 5.3 kPa. He left hospital 2 weeks later. Convalescence was complicated by pulmonary embolism which necessitated a period of treatment with warfarin.

Respiratory function tests 10 months after this episode of life-threatening acute respiratory failure were all within the normal range apart from a reduced carbon monoxide transfer factor. He remains moderately breathless on exertion.

Discussion

A review of the literature by Gille and Bagniewski[1] showed 85% mortality in patients with acute respiratory failure which required treatment with extracorporeal membrane oxygenation (ECMO). The National Heart, Lung and Blood Institute (NHLBI) multicentre, randomised, prospective ECMO study showed that severe, acute respiratory failure treated by conventional means also carries a high overall mortality (91%) which is unaffected by the provision of veno-arterial ECMO.[2]

By contrast, Gattinoni *et al.*[3] achieved a reduction in mortality rate to 51.2% in a single-centre, uncontrolled study in which they employed NHLBI ECMO study entry criteria and a low frequency positive-pressure ventilation protocol (to 'rest the lungs') in association with extracorporeal carbon dioxide removal via veno-venous bypass ($LFPPV-ECCO_2R$).

Our patient met 'fast entry' ECMO study criteria (Pa_{O_2} of less than 6.7 kPa for more than 2 hours on an FI_{O_2} of 1.0 with PEEP of 5 cmH_2O or greater).

An unfavourable prognostic feature was the high prebypass Pa_{CO_2} which Gattinoni *et al.*[3] found to be associated with failure to improve on bypass, presumably because it indicates more serious injury to the pulmonary microvasculature.

However, our patient was young, previously fit, with single organ (lung) failure and with a short prebypass pulmonary insult time in terms of exposure to high inspired oxygen concentration and minute volume (factors known

to cause pulmonary damage). Furthermore, lung inflation pressure never increased to a dangerous level.

These appear to be favourable prognostic features. Nevertheless, Gattinoni *et al.*[3] found no age relationship with mortality, no statistically significant difference between duration of prebypass pulmonary insult in survivor and nonsurvivor groups, and no simple relationship between number of organ failures and mortality (except that there was no survivor with five or more organ failures). However, the spectrum of aetiologies of acute respiratory failure in patients in that study might mask 'within aetiology' mortality trends of this type.

The successful outcome in this case may be associated with the (intuitively) favourable prebypass factors described above, but we would emphasise that, as in Gattinoni's study,[3] we employed veno-venous bypass. This has theoretical advantages over veno-arterial bypass in terms of pulmonary haemodynamics and thus, perhaps, lung tissue nutrition and healing capability. Furthermore, whilst not actually 'resting the lungs' as Gattinoni *et al.*[3] describe, we took care, once bypass was established, to reduce the minute ventilation to the near-normal range, maintained inspired oxygen concentration at 50% or less, restricted PEEP to no more than $5cmH_2O$, and avoided high inflation pressures, so escaping the therapeutic dilemma often encountered of adding insult to injury in the management of severe, acute respiratory failure.

The encouraging results of Gattinoni *et al.*[3] and the evidence of cases such as those described by Gillett *et al.*[4] and ourselves bear witness to the fact that extracorporeal membrane gas exchange remains a potentially life-saving intervention despite the discouraging evidence of the NHLBI ECMO study.

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APPARATUS

The oesophageal detector device

An assessment with uncuffed tubes in children

M. Y. K. WEE AND A. K. Y. WALKER

Summary

In 100 children between the ages of 1–10 years, observers of differing experience reliably and rapidly detected 50 oesophageal and 50 tracheal intubations in a randomised single-blind trial using the original oesophageal detector device. However, only two children under the age of 2 years were tested and no conclusions can be drawn for this age group from this study.

Key words

Equipment; oesophageal detector device.
Anaesthesia; paediatric.

The oesophageal detector device (ODD) has been shown to be a reliable, rapid and easy to use method for distinguishing oesophageal from tracheal intubation in adults intubated with cuffed tubes.[1-4] Detection of oesophageal intubation in children, as in adults, may be difficult and the problem is compounded by their more compliant and thin chest wall. Ventilation through a tube placed in the oesophagus may mimic normal chest movements and auscultation of the chest may fail to detect tube misplacement because of the ready transmission of sound from the oesophagus and stomach to the chest.[5] Furthermore, the initial measurement of end-tidal carbon dioxide may be misleading since carbon dioxide may be forced into the stomach by mask ventilation or from other sources.[6,7] A preliminary study in children between the ages of 5 and 10 years has indicated that the ODD can be used to distinguish oesophageal from tracheal intubation.[8]

Method

One hundred children (ASA 1 and 2) between the ages of 1 and 10 years were included in the study. All were scheduled to have elective surgery where tracheal intubation was required as part of the anaesthetic technique. Children with tracheal, oesophageal or gastric disease were not included in the study. Informed written consent from each child's parent or guardian and local ethics committee approval was obtained.

Routine induction of anaesthesia and tracheal intubation were performed. The tracheal tube was placed to the left or right side of the mouth according to a previously determined randomisation. The oesophagus was than intubated under direct vision using a tube identical to the tracheal tube but positioned to emerge from the opposite side of the mouth.

After optimal oxygenation and maintenance of anaesthesia the breathing system was briefly disconnected from the tracheal tube. An observer, who had not witnessed the positioning of the tube, was required to assess whether the tube in the left side of the mouth was intubating the trachea or oesophagus using the ODD (Fig. 1), as in the original study.[1] The original ODD consists of a 60 ml catheter tip syringe fitted to one end of a catheter mount with a 15 mm female conical tracheal tube connector fitted at the distal end. Aspiration of 5 ml or more of gas should indicate that the tube was in the trachea. The observer was required to aspirate gently and to limit aspiration to 10 ml or less to prevent any possible damage from negative pressure on the tissues.

Documentation included the child's age, size and make of tracheal tube, status of observer, correctness of assessment and time taken, and any adverse sequelae postoperatively.

Results

The ODD reliably and rapidly distinguished oesophageal from tracheal intubation with uncuffed tubes in 100 children between the ages of 1 and 10 years (Table 1), irrespective of the grade of observer (Table 2). The assessments were completed in about 5 seconds and there were no adverse sequelae.

Conclusions cannot be drawn for children between the ages of 1 and 2 years because of the small numbers. A

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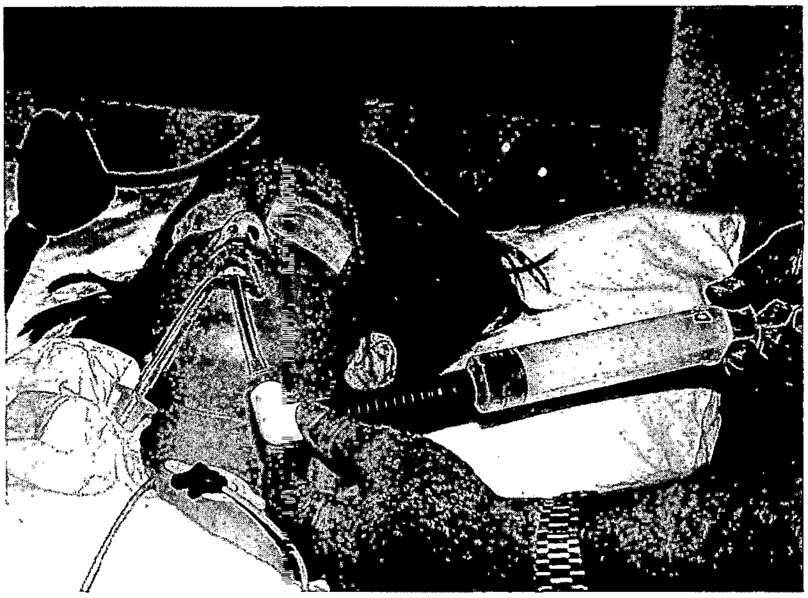

Fig. 1. The oesophageal detector device in use.

recent study of children under 1 year of age showed a modified ODD to be unreliable and various explanations have been put forward.[9] In children between the ages of 2 and 5 years, the observers correctly identified 3 oesophageal and 20 tracheal intubations with no incorrect assessments. In children between the ages of 5 and 10 years the observers correctly identified 16 oesophageal and 27 tracheal intubations; this confirmed the reliability of the ODD in this age group.

Discussion

It was noted that the recommended aspiration volume of less than 10 ml allowed clear differentiation between oesophageal and tracheal placement. The observation with these small volumes, however, may be facilitated by performing the test with the plunger positioned from the 10 ml mark on the syringe rather than the zero mark. This will prevent the initial suction effect of the syringe plunger against the syringe wall.

The RAE tube has a side hole (Murphy's eye) approximately 1 cm from the tip of the tube. If an inappropriately small tube is placed in the oesophagus, part of the side hole may remain outside the oesophagus and allow free aspiration of air through the side hole, to give a false assessment; this did not occur in this study. It is recommended that the ODD should be used before any insufflation through the tube since air or gases in the oesophagus could produce a false result, particularly with the small aspiration volume recommended in children. The use of the original ODD (60 ml catheter tip syringe, catheter mount and 15 mm connector) was satisfactory in children as the large syringe resulted in less negative pressure applied to the airway than when a smaller syringe was used.

Finally, it is important to check that there are no leaks in the ODD before use and that the connexion between the device and the tube is airtight. This can be easily done by occluding the distal end with a thumb and pulling back on the plunger.

It would seem from this study that the original ODD may be of potential use in distinguishing oesophageal from tracheal intubation in children between the ages of 2 and 10 years and further clinical evaluation of its use is warranted.

Table 2. Grade of observer using the oesophageal detector device.

Anaesthetists:	Consultants	34
	Registrars	22
	Senior House Officers	28
Other personnel:	Operating Department Assistants	14
	Ambulance Paramedics	2

Table 1. Patient data and results.

Age range (years)	Oesophageal tubes (n)	Tracheal tubes (n)	Correct (n)	Incorrect (n)	Approximate time taken (seconds)	Uncuffed RAE tube sizes (mm ID)
1–2	1	1	2	0	5	4.0, 4.5
2–5	31	20	51	0	5	4.5, 5.0
5–8	17	22	39	0	5	5.5, 6.5
8–10	1	7	8	0	5	6.0, 6.5, 7.0
Totals	50	50	100			

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APPARATUS

Identification of the epidural space in children

The application of a micro-drip infusion set

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Summary

We have used an intravenous micro-drip infusion set to identify the epidural space in 350 infants and children. The infusion set was prepared with saline and connected to the hub of an epidural needle. Free dripping of saline was regarded as a sign that the needle tip had entered the epidural space. The overall success rate of this method was 97.7%.

Key words

Anaesthesia; paediatric.
Anaesthetic techniques, regional; epidural.
Equipment; micro-drip infusion set.

The use of lumbar and thoracic epidural anaesthesia for operations on infants and children was first reported more than 35 years ago.[1] Several reports of the use of this technique in infants and children, including more than 10 000 cases in China, have been published recently,[2–6] but epidural anaesthesia seems not to be popular in this age group at present. One possible reason for its unpopularity is difficulty in locating the epidural space, with the risk of accidental production of a total spinal block.[7] We have used a micro-drip infusion set, as described in adult patients,[8,9] in infants and children in order to facilitate identification of the epidural space.

Methods

Identification of the epidural space by the micro-drip infusion set has been used in 350 infants and children under 9 years of age. The sites of puncture were in the lumbar region in 300 cases and in the thoracic region in 50 cases. The age distribution is shown in Tables 1 and 2.

A sterile intravenous micro-drip infusion set, prepared with saline as for an intravenous infusion, was added to the standard epidural tray. Epidural puncture was performed during general anaesthesia provided by halothane.

The tip of the epidural needle was inserted into the interspinous ligament, the stilette removed and the distal end of the infusion set connected to the needle hub. The micro-drip chamber was kept about 1 metre above the puncture site. The clamp of the infusion set was opened fully; no dripping should be observed if the tip of the needle is in the interspinous ligament. An assistant observed the drip chamber while the needle was advanced slowly and carefully by the anaesthetist. At the first sight of dripping (an objective sign of loss of resistance), the anaesthetist was notified immediately. He stopped advancing the needle, confirmed free flow of fluid in the drip chamber, and closed the clamp. Usually, movement of a tiny air bubble at the hub of the epidural needle (transparent hub) towards the epidural space can be observed by the anaesthetist.

Correct placement of the needle was confirmed using a standard method[10] before administration of local anaesthetic solution or insertion of an epidural catheter. Bupivacaine (0.25%) with 1:200 000 adrenaline was administered in a volume of 0.75 ml/kg in the lumbar region, and of 0.4–0.5 ml/kg in the thoracic region.[4] The identification of the epidural space was judged correct when the following criteria were met: no dripping of cerebrospinal fluid (CSF); no increase of heart rate or blood pressure and no body movement on skin incision under general anaesthetic with nitrous oxide and oxygen (2:1) and halothane 0.5% following administration of local anaesthetic, i.e. clinically effective epidural anaesthesia.

Results

The epidural space was located accurately by this method in 342 cases (97.7%). Inadvertent dural puncture was identified by the dripping of CSF in four cases, all using the lumbar approach (two in children aged one month, one

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Table 1. Age distribution and success rate of identification of the epidural space in infants and children.

Age (years)	<1	1	2	3	4	5	6	7	8	Total
Lumbar approach	119	55	28	31	21	23	13	5	5	300
Thoracic approach	36	5	3	0	0	3	1	1	1	50
Total number	155	60	31	31	21	26	14	6	6	350
Dural punctures	4*		1							5
Clinically ineffective epidural anaesthesia	1	1			1					3
Success rate (%)†	97	98	97	100	95	100	100	100	100	97.7

*Including one possible subdural injection of local anaesthetic.
†Success rate of correct identification of epidural space without preceding dural puncture, which resulted in clinically effective epidural anaesthesia.

Table 2. Age distribution of children aged less than one year.

Age (months)	<1	1	2	3	4	5	6	7	8	9	10	11	Total
Lumbar approach	13†	19*‡	21*	9	10	5	10	5	6	4	10	7	119
Thoracic approach	10	16	4	1	1	0	2	0	0	1	1	0	36
Total number	23	35	25	10	11	5	12	5	6	5	11	7	155

*Dural puncture.
†Possible subdural injection.
‡Clinically ineffective epidural.

aged 2 months and one aged 2 years). Three of the four dural punctures occurred within the first 30 cases in the series. One possible subdural extra-arachnoid injection of local anaesthetic solution occurred in a one-day-old neonate; no dripping of CSF was noticed, but after the injection of local anaesthetic, respiratory arrest occurred and an unusually high sensory blockade was observed. The neonate recovered without adverse sequelae after 6 hours of mechanical ventilatory support.

Clinically ineffective epidural anaesthesia occurred in three patients, one aged one month, one aged one year and one aged 4 years. Most of the thoracic approaches in patients younger than 3 months old were for pyloromyotomy. Most of the lumbar approaches in neonates were for colostomy, or repair of umbilical hernia.

Discussion

This method of identification of the epidural space using a micro-drip infusion set is useful and reliable in infants and children. There are several advantages over traditional loss-of-resistance methods using air or saline. Firstly, an epidural needle with wings can be advanced with both hands; precise control of movement is easier by this method than by the loss-of-resistance method, where one hand holds the needle and the thumb of the other hand pushes the piston of the syringe. Secondly, air is not injected into the epidural space. Air bubbles in the epidural space have been reported to be the cause of incomplete analgesia during epidural anaesthesia.[11,12] In addition, air in the epidural space has been blamed for lumbar root compression,[13] subcutaneous emphysema,[14] and interscapular pain.[15] These complications can be prevented with our method. Thirdly, only a very small amount of saline is infused into the epidural space, so dilution of the local anaesthetic is minimised.

Inadvertent dural puncture occurred in three infants in the early part of this series. At this time, only adult-sized winged 8-cm (20-gauge) single-shot epidural needles were available. Currently, we use 3.5 cm 20-gauge winged single-shot epidural needles (Hakko-Syouji, Tokyo, Japan) for infants and small children, and 6 cm 20-gauge winged single-shot epidural needles for older children. We believe that the use of the correct size of needle and our method of identification of the epidural space improves the success rate of epidural anaesthesia in infants and children.

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Forum

Rectus sheath and mesosalpinx block for laparoscopic sterilization

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Summary

Thirty patients scheduled to undergo laparoscopic sterilisation were allocated at random to receive either a standardised general anaesthetic and rectus sheath block (group A), or standardised general anaesthetic combined with both rectus sheath and mesosalpinx blocks (group B). Group B patients had significantly less postoperative pain, as assessed by linear analogue scores ($p < 0.025$), and analgesic requirement ($p < 0.05$). By the 8th postoperative hour all 15 group B patients had been discharged from hospital, whilst only seven of 15 patients in group A were considered suitable for discharge at this time. ($p < 0.05$).

Key words

Anaesthetic techniques, regional; rectus sheath block, mesosalpinx block.
Surgery; laparoscopy.
Pain; postoperative.

Following the demonstration that the use of bilateral rectus sheath block can reduce significantly postoperative pain after diagnostic laparoscopy,[1] the same technique was applied in patients undergoing laparoscopic sterilisation. During the course of a pilot study it became clear while abdominal wall pain was obtunded, most patients complained of deep pelvic pain, similar to dysmenorrhoea. As these symptoms had not been reported during the diagnostic laparoscopy study, but had been observed by gynaecologists following sterilisation with Falop rings in other patients, we concluded that they were probably attributable to the occlusion of the Fallopian tube. The Fallopian tube has no demonstrable somatic nerve supply, but has autonomic innervation via the mesosalpinx. Local anaesthetic blockade of the mesosalpinx adjacent to the point of Fallopian occlusion should interrupt autonomic afferents and prevent perception of pain. This study was undertaken to test this hypothesis in the clinical situation.

Patients and methods

The study was approved by the district ethics committee and 30 patients of ASA grades 1 or 2 scheduled to undergo laparoscopic sterilisation were investigated. Formal consent was obtained from the patients following both verbal and written description of the proposed research. All patients were admitted as unpremedicated day cases and were allocated to either group A or group B on the basis of a random number sequence.

Group A patients received a standardised general anaesthetic sequence comprising alfentanil 30 μg/kg, propofol 2.5–3.0 mg/kg and vecuronium 0.1 mg/kg. The trachea was intubated and anaesthesia maintained with 66% nitrous oxide in oxygen, with 0.5% halothane if clinically indicated. Bilateral rectus sheath block was performed using a mixture of equal parts of prilocaine 1% and bupivacaine 0.5% without adrenaline, in a volume of 0.25 ml/kg per side.[1] Neuromuscular block was antagonised at the end of the procedure with neostigmine 50 μg/kg and glycopyrronium 20 μg/kg. In group B, an identical sequence of general anaesthesia and rectus sheath block was employed. In these patients mesosalpinx block was performed under direct vision by the surgeon at laparoscopy.

Technique of mesosalpinx block. A standard two-puncture laparoscopic technique was used with carbon dioxide as the insufflating gas. Each Fallopian tube was identified and ligated with a Falop ring 2–3 cm from the uterine cornu. With the tube still held in the ring applicator forceps, a 20 gauge × 5 inch (12.5 cm) spinal needle was inserted 3 cm above and 5 cm lateral to the pubic symphysis on the appropriate side. The needle was advanced under direct vision, through the posterior leaf of the mesosalpinx about 1 cm below the position of the Falop ring and 2–3 ml of bupivacaine 0.5% without adrenaline injected. At the end of the procedure the pneumoperitoneum was reduced as far as possible before withdrawing the laparoscope sheath.

Analgesic prescribing All patients were prescribed intramuscular papaveretum 0.25 mg/kg 3-hourly as required and oral dihydrocodeine 60 mg 4-hourly as required. The decision to administer analgesia and the choice of analgesic were left in the hands of the nursing staff, who were blind to the patient grouping.

Postoperative assessment All patients were assessed by an independent observer at 1 and 4 hours postoperatively, and again at 8 hours after operation if they had not been discharged. The decision to discharge the patient was left to the anaesthetic and gynaecology junior staff, who were blind to the patient grouping. (The protocol allowed for

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Table 1. Visual analogue scores at each postoperative assessment, where 0 represents no pain and 10 severe pain. Figures are means (range).

	Group A (control) $n=15$	Group B (study) $n=15$	p
1 hour	5.24 (1.8–8.3)	1.83 (0.6–3.7)	<0.025
4 hour	2.77 (1.6–5.2)	1.13 (0.3–1.9)	<0.025

Table 3. One hour postoperative assessment. Number of patients in each group who complained of postoperative pain according to site.

	Group A	Group B	p
Abdominal wall pain	1	2	ns
Pelvic pain	11	1	<0.025
Shoulder pain	2	3	ns
Other pain	3	2	ns

Table 4. Four hour postoperative assessment. Number of patients in each group who complained of postoperative pain according to site.

	Group A	Group B	p
Abdominal wall pain	1	1	ns
Pelvic pain	8	0	<0.025
Shoulder pain	1	1	ns
Other pain	2	2	ns

discharge at any time after four hours.)

The assessment comprised three separate parts: first 10 cm visual analogue score lines, where 0 represented no pain and 10 severe pain; second, direct questioning of the patient regarding the presence and severity of pain according to site, namely abdominal wall pain, pelvic pain, shoulder pain and pain in any other area. The observer was asked to grade any reported pain on a three-point scale of mild, moderate or severe. Finally, any administration of analgesic was recorded. The data were analysed using the Wilcoxon rank sum test, analysis of variance and the Chi-squared test (with Yates' correction) as appropriate.

Results

There were no statistically significant differences between the groups in terms of age, weight or ASA status. Only three patients, two in group A and one in group B were given halothane during the procedure. The visual analogue scores for the 1 and 4 hour assessments are shown in Table 1. The 8 hour assessment is not shown since all group B patients were discharged before this assessment. The difference between the groups is statistically significant at both 1 and 4 hours ($p < 0.025$ in each case).

The results of direct questioning at 1 and 4 hours are shown in Tables 2 and 3 respectively. The lower incidence of pelvic pain in group B was significant at both assessments. The severity scores in both assessments were statistically significant, but the imprecision of this assessment precludes the drawing of valid clinical conclusion and are not therefore presented. The results for analgesic administration are shown in Table 4. The lower incidence of papaveretum administration in group B during the first 4 hours is statistically significant and there was a significant difference between the groups in terms of patient discharge. In group A, the mean time to discharge was 7.68 hours (range 5.5–12), while the corresponding figure for group B was 4.86 hours, (range 4.25–6.5) $p < 0.025$.

Discussion

The use of rectus sheath block significantly reduces the incidence of postoperative pain following simple laparoscopy,[1] but our experience showed that this was not the case with laparoscopic sterilisation. Most patients in our pilot study required intramuscular analgesia, and were not suitable for same-day discharge. This study demonstrates that if bilateral mesosalpinx block is included in the anaesthetic technique then not only is postoperative pain significantly reduced, despite the greater use of opioid analgesics in group A, but day case admission is entirely feasible.

Other techniques to reduce pelvic pain have been suggested and include topical application of local anaesthetics, particularly etidocaine, to the pelvic viscera,[2,3] and more recently, per-cervical administration of bupivacaine.[4] Both techniques appear to reduce postoperative pain, although the dose of local anaesthetic used in the intra-abdominal method was relatively high at 2 mg/kg of etidocaine, or 1.5 mg/kg of bupivacaine. It is interesting that the study by McKenzie *et al.*[2] reported the abolition of all postoperative pain in over two-thirds of patients in the etidocaine-treated group, despite the absence of any specific block of the laparoscope entry site. Why this should be so is unclear. A similar result has been claimed for the per-cervical route of administration with 10 ml of bupivacaine 0.5%; only six of 22 patients needed additional analgesia, again without block of the abdominal entry site.[4]

The studies quoted above were based on assessments made during the first 2 hours after operation. The duration of analgesia in either study is not reported. In the present study, several patients in group A required intramuscular analgesia more than 4 hours after operation, and oral analgesia more than 8 hours postoperatively. This suggests that any local technique used to reduce pelvic pain should last for at least 4 hours and preferably more than 8 hours. Although not formally studied, informal follow-up of group B patients suggested that the duration of action of the mesosalpinx block ranged from 6 to 14 hours.

The technique of mesosalpinx block is not difficult to learn, although it adds 3 or 4 minutes to the total operation

Table 2. Analgesic requirements for each group during three time bands.

	Group A		Group B	
	Papaveretum	Codydramol	Papaveretum	Codydramol
0–1 hour	6	3	1	3
1–4 hours	5	5	0	2
4–8 hours	3	4	0*	3*

*All patients in group B were discharged by 6.5 hours after operation.

time. The only complication of the block seen in this series was of minor bleeding from the mesosalpinx when observed at laparoscopy. This occurred in two otherwise normal patients, and in neither case was specific treatment at the time of operation required, although one patient needed one dose of papaveretum after operation for unilateral pelvic pain. There were no other adverse effects observed attributable to either the rectus sheath or mesosalpinx blocks.

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Cardiovascular changes at antagonism of atracurium

Effects of different doses of premixed neostigmine and glycopyrronium in a ratio of 5:1

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Summary

The cardiovascular changes in the 10 minutes following antagonism of an atracurium-induced block were studied in 32 patients. A 5:1 ratio combination of either 15, 35, 55 or 75 μg/kg neostigmine, with a corresponding dose of 3, 7, 11, or 15 μg/kg of glycopyrronium was used for antagonism. The least change in heart rate was with neostigmine 15 μg/kg with an increase of more than 15 beats/minute found in only one patient. Antagonism with 35, 55 and 75 μg/kg neostigmine mixture produced the greatest increase in heart rate at one minute and this was significantly different from the effect of the 15 μg/kg dose. Twenty out of 24 patients given the larger doses had heart rate increases in excess of 15 beats/minute and in nine patients this ranged from 30 to 52 beats/minute, representing increases of 46–80% above baseline values. Arterial pressure increases after antagonism were statistically significant in all four groups, with no between-group difference; these were clinically unimportant. When antagonising an atracurium-induced block with clinically useful doses of neostigmine, the standard 5:1 ratio combination with glycopyrronium will result in an initial tachycardia.

Key words

Antagonists; neuromuscular relaxants, neostigmine.
Parasympathetic nervous system; glycopyrronium.
Neuromuscular relaxants; atracurium.

Since its introduction into the United Kingdom in 1987, a commercial mixture of neostigmine and glycopyrronium has been popular for antagonism of neuromuscular blockade. Its advantages over the traditional combination of atropine and neostigmine include convenience of administration, better control of secretions, lower incidence of arrhythmias and a faster arousal and return of cognitive functions after general anaesthesia.[1–6]

Ramamurthy *et al.* first investigated the optimal combination of neostigmine and glycopyrronium for reversal of a pancuronium-induced block.[7] A ratio of 5:1 was associated with the most stable heart rate (HR), and this was subsequently confirmed by Mirakhur *et al.*[8] However, neither glycopyrronium nor neostigmine has a linear dose-related effect on the HR, and it is possible that cardiac responses will not be constant over the range of clinically relevant doses of this mixture. This study was therefore undertaken to investigate the cardiovascular effects of the

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Table 1. Demographic data showing the mean (SD); n = the number of patients in each group. Neostigmine was in a premixed 5:1 ratio combination with glycopyrronium.

	n	Age; years (SD)	Weight; kg (SD)	Sex M/F
Group 1; neostigmine 15 μg/kg	8	27.2 (8.9)	60.7 (4.9)	2/6
Group 2; neostigmine 35 μg/kg	8	30.5 (9.9)	68.2 (10.1)	4/4
Group 3; neostigmine 55 μg/kg	8	27.6 (10.1)	66.5 (7.5)	2/6
Group 4; neostigmine 75 μg/kg	8	29.2 (7.3)	70.7 (12.2)	3/5

premixed 5:1 ratio combination of neostigmine and glycopyrronium during antagonism of an atracurium-induced block, at doses of neostigmine ranging from 15 to 75 μg/kg.

Methods

Thirty-two ASA 1 patients undergoing elective oral surgery were divided at random into four equal groups. Ethics committee approval and informed consent were obtained. Patients on medication known to affect neuromuscular or cardiac function were excluded.

Premedication was with intramuscular papaveretum (15–20 mg) and hyoscine (0.3–0.4 mg) given one hour before surgery. Anaesthesia was induced with fentanyl (1–2 μg/kg) and thiopentone (4–6 mg/kg) and maintained with isoflurane and 66% nitrous oxide in oxygen. After neuromuscular monitoring was established, atracurium in a dose of either 0.35 mg/kg or 0.4 mg/kg was given to facilitate intubation and controlled ventilation. A Datex Normacap was used to maintain end-tidal carbon dioxide concentration between 4.5 and 5.3 kPA, while a Datex Normac ensured stable end-tidal isoflurane concentrations at 0.5%. A Datex relaxograph was used to stimulate the ulnar nerve at the wrist with impulses of 0.1 msecond duration delivered as a train-of-four (TOF) at 2 Hz every 10 seconds. The integrated evoked compound electromyogram was measured over the adductor policis muscle and recorded on a Gould chart recorder. The arm used for recording was wrapped in cotton wool and palm temperature was maintained at 34–37°C.

Neuromuscular block was allowed to recove spontaneously until the first response (T1) of the TOF was approximately 10% of control response height. At this point, under stable anaesthesia, patients received either 15, 35, 55 or 75 μg/kg of neostigmine with the corresponding dose of 3, 7, 11, or 15 μg/kg of glycopyrronium. Anaesthesia was continued throughout the period of neuromuscular recovery.

The ECG was continuously recorded onto a paper trace and the heart rate was calculated from the interval between five R-R complexes at −1, −0.5, 0, +0.5, +1 minute, and then at one-minute intervals for 10 minutes after antagonism. Arrhythmias were noted and recorded, as was the noninvasive blood pressure (BP) measurement recorded with a Datascope Accutor at one minute intervals during the period of study.

Statistical analysis

Repeated measures analysis of variance (RM ANOVA) was used to analyse changes in HR and systolic and diastolic blood pressure over time and between groups. The conservative method of Greenhouse and Geisser was used to determine significance.[9] Baseline values and the values at one minute after antagonism were compared between the groups with analysis of variance. Where a significant difference was found, the Student–Newman–Keuls (S–N–K) test was used to identify differences between the groups. Student's paired t-tests compared baseline HR with values at one minute following antagonism within each group. $p < 0.05$ was accepted as significant.

Results

There were no statistically significant differences with regard to age, sex, weight, pre-reversal heart rates or systolic and diastolic blood pressures in the groups (Tables 1–3). RM ANOVA demonstrated a significant difference over time for all four groups analysed together ($p < 0.0001$). There was also a significant difference between the four groups ($p = 0.014$), but not between the groups given the three larger doses of neostigmine (35 to 75 μg/kg). At

Table 2. Prereversal values (mean (SEM)) at −1 minute for systolic and diastolic BP, and time to TOF ratio = 0.9 following antagonism in the four groups. Neostigmine was in a premixed 5:1 ratio combination with glycopyrronium.

	Prereversal		
	Systolic BP (mmHg)	Diastolic BP (mmHg)	Time to TOF ratio = 0.9 (minute)
Group 1; neostigmine 15 μg/kg	112.1 (5.3)	69.4 (3.9)	16.5 (1.2)
Group 2; neostigmine 35 μg/kg	117.8 (8.3)	74.8 (4.5)	10.3 (0.7)
Group 3; neostigmine 55 μg/kg	118.8 (6.4)	77.1 (4.5)	10.1 (1.4)
Group 4; neostigmine 75 μg/kg	118.5 (11.9)	77.0 (8.4)	9.9 (1.0)

Table 3. Heart rate (mean (SEM)) before and following antagonism with neostigmine and glycopyrronium in a ratio of 5:1. Antagonist administered immediately after time 0.

	Heart rate beats/minute											
	−1 min	0	+1 min	2 mins	3 mins	4 mins	5 mins	6 mins	7 mins	8 mins	9 mins	10 mins
Group 1; neostigmine 15 μg/kg	76.0	74.8	80.8	77.8	76.0	75.7	75.1	71.7	73.7	71.2	73.7	70.3
	(4.7)	(4.4)	(5.7)	(5.9)	(5.1)	(4.6)	(4.8)	(4.8)	(3.8)	(3.4)	(2.9)	(3.5)
Group 2; neostigmine 35 μg/kg	64.5	63.5	87.2	85.3	79.3	76.2	75.1	74.5	75.6	74.6	72.2	73.5
	(2.7)	(2.3)	(4.1)	(3.4)	(3.1)	(2.9)	(3.1)	(3.1)	(3.8)	(3.5)	(2.8)	(3.8)
Group 3; neostigmine 55 μg/kg	69.4	72.0	103.0	97.2	92.5	88.5	85.3	83.7	82.5	81.1	80.4	77.6
	(3.1)	(3.9)	(5.5)	(5.5)	(5.9)	(5.6)	(4.9)	(4.9)	(5.3)	(4.7)	(5.2)	(4.5)
Group 4; neostigmine 75 μg/kg	66.7	65.0	94.8	89.5	86.3	83.0	81.8	79.3	77.1	76.1	75.0	73.2
	(3.0)	(2.6)	(6.3)	(6.2)	(6.2)	(6.1)	(5.4)	(5.4)	(5.6)	(5.8)	(6.3)	(6.2)

one minute following reversal, the HR of patients given neostigmine 15 μg/kg were significantly different (S–N–K) from the other groups, but not from its prereversal value. HR of patients in the other groups at one minute (35 to 75 μg/kg) were significantly greater than baseline. A bradycardia (HR less than 50 beats/minute after antagonism) of 48 beats/minute was recorded in just one patient in whom the prereversal HR was 58 beats/minute; this was in the 75 μg/kg group at the 10th minute following antagonism. A maximum increase in HR of more than 15 beats/minute was found in only one patient in the 15 μg/kg group, whereas 20 of the remaining 24 patients had increases of this magnitude or higher. In about 50% (nine patients) of this latter group, increases in HR ranged from 30 to 52 beats/minute, representing increases of 46–80% above baseline values.

There was a significant change over time in both systolic and diastolic arterial pressures following antagonism in all four groups, but no difference between the groups was detected in this change.

Arrhythmias following antagonism were mainly junctional rhythm or isolated atrial ectopic beats or a combination of the two. These were noted in seven patients; once in the 15 μg/kg group, and in two patients in each of the three remaining groups. No ventricular ectopic beats were recorded.

Discussion

The cardiovascular responses during antagonism of neuromuscular block depend on several factors. These include the prevailing vagal activity, which is higher in young, fit adults than at the extremes of age.[10,11] The anaesthetic technique, in particular the choice of inhalational agent and the muscle relaxant employed, will also modulate this response.[12–14] The optimal dose of an anticholinergic agent for prevention of undesirable muscarinic effects in combination with an anticholinesterase, is one that will result in neither undue initial tachycardia nor in subsequent bradycardia. The combination of atropine and neostigmine is associated with cardiovascular instability, while glycopyrronium, when substituted for atropine, reduces the incidence of these fluctuations.[1,2,7,15]

We found that a dose of neostigmine 15 μg/kg in combination with glycopyrronium 3 μg/kg was associated with the least increase in HR when antagonising an atracurium-induced block (Fig. 1). The apparently high baseline HR in this group is accounted for by a prereversal HR of 101 beats/minute in one patient and the absence, in contrast to the other groups, of HR values below 60 beats/minute. One patient, in whom monitoring was discontinued at a TOF ratio of 0.87, failed to recover to a TOF ratio of 0.9. Times to this target ratio were approximately 6 minutes longer than the other three groups (Table 2) and this dose might well be considered inadequate for routine antagonism of neuromuscular blockade.

The larger, more clinically useful doses of this mixture, from 35–75 μg/kg of neostigmine resulted in a significant increase in HR within one minute. In individual patients, HR rose by up to 52 beats/minute representing an 80% increase from prereversal value. Prereversal HR and blood pressure (Table 2) were stable; no teeth were extracted during the period of study and antagonism occurred under stable and constant anaesthesia. An obvious and significant difference in HR response was noted when compared with the neostigmine 15 μg/kg group.

The initial increase in HR in these three groups resembles the effect of atropine in the early studies, when atropine was compared with glycopyrronium.[7,15] The potentially deleterious effects of such atropine-induced tachycardia were generally considered to be of little clinical consequence; but marked changes in heart rate during reversal, especially in patients with pre-existing cardiac disease, have subsequently been shown to result in arrhythmias and ischaemic ECG changes.[16,17] Abrupt increases in HR, as noted in patients receiving the larger doses of the 5:1 mixture (35–75 μg/kg neostigmine and glycopyrronium 7–15 μg/kg) would therefore raise identical concerns.

The tachycardia seen in our patients has not been reported before with comparable doses of the same ratio of neostigmine and glycopyrronium. This may be because pancuronium, with its well known vagolytic and sympathomimetic effects[18,19] was the muscle relaxant commonly used in previous studies. When comparing similar doses of a 5:1

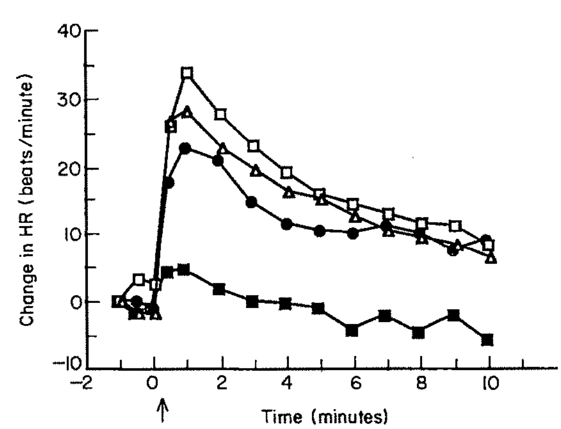

Fig. 1. Change in heart rate (HR) following antagonism with neostigmine and glycopyrronium in a ratio of 5:1. Neostigmine 15 μg/kg, solid squares; neostigmine 35 μg/kg, solid circles; neostigmine 55 μg/kg, open squares; neostigmine 75 μg/kg, triangle. Arrow indicates time of injection of reversal mixture. HR values in Table 3.

mixture of neostigmine and glycopyrronium (0, 60, 80 μg/kg of neostigmine) no initial tachycardia or difference in HR response was detected at antagonism of a pancuronium-induced block.[20] During isoflurane anaesthesia, vecuronium is associated with lower HR than pancuronium.[21] Atracurium may be similar to vecuronium in this respect since it is largely devoid of cardiovascular effects in the doses used in this study. It is therefore possible that this clean cardiovascular profile of atracurium,[22,23] unmasks the tachycardic effects of the 5:1 ratio combination of neostigmine and glycopyrronium when using doses of 35–75 μg/kg neostigmine for antagonism of neuromuscular blockade.

Arterial pressure changes, although small, were statistically significant because almost all changes occurred in the same direction. The maximum individual increase in either systolic or diastolic pressures in the four groups did not exceed 15% of baseline values. Clinically, these changes were therefore unimportant.

Glycopyrronium results in fewer arrhythmias than atropine when combined with neostigmine.[1–3,24] Arrhythmias noted in the seven patients following antagonism in this study either reverted spontaneously to sinus rhythm, or when persistent, were of no haemodynamic consequence. No ventricular ectopic beat was noted.

We conclude that neostigmine 15 μg/kg and the corresponding dose of glycopyrronium 3 μg/kg in the premixed commercially available combination, is not associated with significant change in HR following antagonism of an atracurium-induced block. However, this dose is too small for routine reversal and would seem to be indicated only in clinical situations where cardiovascular stability is crucial and where antagonism is preferred to spontaneous recovery of neuromuscular blockade.

The higher doses of neostigmine and glycopyrronium were associated with HR increases of 46–80% above prereversal values. This suggests that the currently accepted 5:1 ratio of neostigmine and glycopyrronium may be inappropriate when antagonising the present generation of cardiostable relaxants such as atracurium. It is possible that less glycopyrronium with clinically useful doses of neostigmine will result in reduced initial tachycardia and such a combination requires evaluation.

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Topical glyceryl trinitrate and eutectic mixture of local anaesthetics in children

A randomised controlled trial on choice of site and ease of venous cannulation

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Summary

One hundred and four children aged between 1 and 11 years were studied in a double-blind randomised controlled trial of glyceryl trinitrate ointment versus placebo, when used in addition to standard eutectic mixture of local anaesthetics cream. Each child received glyceryl trinitrate ointment on one hand and placebo on the other, and thus acted as his/her own control. A group of 30 children who received only the eutectic mixture on both hands (60 measurements) was also studied. The choice of site and ease of cannulation was scored. Skin colour and venous dilatation under the eutectic mixture were scored on a visual analogue scale. The addition of topical glyceryl trinitrate ointment to the standard eutectic mixture positively affected venous dilatation ($p < 0.01$), choice of cannulation site ($p < 0.001$), and ease of cannulation ($p < 0.001$) of topical anaesthetic-treated skin.

Key words

Anaesthesia; paediatric.
Anaesthesia, local; EMLA.
Pharmacology; glyceryl trinitrate.

Topical application of a eutectic mixture of local anaesthetics (EMLA) reduces the pain of venous cannulation, but has also been reported to cause blanching of skin, local pallor, vasoconstriction and difficulty with venepuncture.[1–4] Glyceryl trinitrate (GTN) ointment has been used topically to facilitate intravenous access in adults and children. The dose for children has been 0.4 to 0.8 mg with a suggested application time of 20 minutes to 2 hours, although the maximum haemodynamic effect when used as treatment for cardiac conditions is at 30 minutes.[5–10] The aim of this study was to determine if the addition of topical GTN would affect the choice of site and ease of venous cannulation in children.

Methods 1

Pilot study. A pilot project was carried out in order to study the effects of topical GTN ointment on (a) the analgesic onset, intensity and duration of standard EMLA cream treatment and (b) colour and vein dilatation of EMLA-treated skin. A double-blind, randomised own-controlled trial was performed on 10 volunteer adults using standard EMLA cream test patches and pinprick, using the methods of Evers *et al.*[3] GTN ointment 0.4% was compared with placebo ointment applied as a patch distal to the EMLA patch. This was because a diminution of analgesic effect was found in preliminary tests if EMLA was in contact with GTN ointment or placebo. This could be the result of dilution or adsorption of EMLA in an oil-base ointment. The results showed that the onset, intensity and duration of analgesia was not affected by topical GTN. In eight of the subjects, the veins on the GTN-treated hand were judged to be more dilated than the placebo-treated hand. In two subjects, the vasodilatation was judged equal on both sides. None of the subjects had more vasodilatation on the placebo-treated hand. There was a statistically significant improvement in the skin colour score with the addition of topical GTN to standard EMLA treatment. The pilot study was used to calculate the sample size needed to detect differences of clinical importance for the main trial.

Methods 2

Patients and clinical methods. The study, a double-blind randomised self-controlled trial, was approved by the Area Health Authority Ethics Committee. Written informed parental consent was obtained. Healthy ASA 1 and 2 children aged between 1 and 11 years who were scheduled for minor ear, nose and throat surgery were entered in the trial. All the children received oral trimeprazine 2 mg/kg and oral atropine 0.1–0.3 mg as premedication.

The test preparations were: proprietary EMLA cream; 0–4% GTN ointment produced by the hospital pharmacy by diluting 2% GTN ointment with lanolin and lactose; placebo ointment of lanolin and lactose. The GTN and placebo ointments were supplied as paired coded packages and each pair used for one theatre session only. All the children received EMLA cream as recommended by the manufacturers on the dorsum of each hand. In addition, the main group of 104 children received 0.2 ml of the 0.4% GTN ointment, as a smeared patch, distal to the EMLA patch on one hand; 0.2 ml of placebo ointment was applied as a patch distal to the EMLA patch on the other hand. The GTN patch (0.8 mg) was placed distally to prevent adsorption of EMLA into oily ointment or dilution effect (Fig. 1).

An EMLA-only group of 30 children received EMLA cream only. This was to compare with the placebo hands of the main group which may have been affected by systemic effects of GTN from the contralateral hand. The ointments

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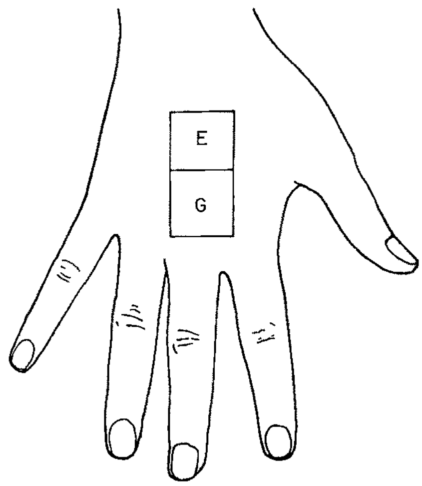

Fig. 1. Dorsum of hand showing EMLA patch (E) and GTN or placebo patch (G).

and creams were then covered with a plastic occlusive dressing (Tegaderum) for a minimum of 45 minutes.

Randomisation was achieved by assigning alpha-numeric codes to the pairs of ointments which were changed on a daily basis at random, e.g. AB1 and AB2; PQR1 and PQR2. The numeric component of the code was assigned at random to both GTN and placebo. This elaborate coding was instituted so that the nurse applying the ointments was not burdened with the workload of randomisation on the ward, and had free choice as to which ointment to apply to each hand as long as they were pair-coded. Both hands received EMLA patches, which the nurse centred over the best vein of each hand, if visible; otherwise the centre of the dorsum of the hand was used. The position of patches was remarkably consistent because of the constraint of physical size of the plastic dressing in relation to available surface area on the child's hand. As both hands received EMLA patches, the choice of side for cannulation by the anaesthetist should have been influenced only by the GTN or placebo. There was equal chance of the 'good' or 'bad' preoperative veins receiving GTN or placebo.

Demographic details, time of application of ointments and the code for each hand was noted on the nurses' datasheet. The anaesthetist had no access to this and used a separate doctors' datasheet for the observations. The observations were mainly made by one of two consultant anaesthetists and consisted of: time of removal of ointments; colour of skin under the EMLA patch; dilatation of veins under the EMLA patch; choice of hand for cannulation; this choice excluded ergonomic or surgical considerations; side effects; headaches and hypotension were specifically asked for; site and number of cannulation attempts; ease of cannulation; and final side cannulated and anaesthetic induction method. The colour and vein dilatation was scored on a 100 mm visual analogue score (VAS) for each hand. These were ungraduated 100 mm lines with the following scales: VAS colour: 0 = white, 50 = normal, 100 = red; VAS dilatation: 0 = poor, 50 = normal, 100 = good.

At the start of the trial, one of the authors (W.L.M.T.-F.) jointly made the scoring observations with the anaesthetists, and attempted to standardise the scoring. The vein was punctured at the site of the EMLA patch. The ease of cannulation for each attempt was scored as one of the following: easy, moderate, difficult. The protocol allowed the anaesthetist to make the cannulation attempt on either hand so that the visually better hand may not have been used. The data for number and ease of cannulation attempts are thus analysed separately as populations of hands with any of the three treatments applied: EMLA only, EMLA–GTN, EMLA–placebo.

Statistical methods. The sample size (n) needed to detect clinically important differences in dilatation scores of at least 15 between the EMLA–GTN and EMLA-only measurements with 80% power was calculated to be about 60. These calculations were based on a two-tail test at 5% significance level with scores normally distributed with standard deviation equal to 30. A larger sample (104) was taken for the EMLA–GTN experimental group. The Kolmogorov-Smirnov (K-S) test for normality of distributions was applied to the data groups and their differences. The z-test, the two-sample t-test, and the Wilcoxon matched-pairs signed rank test were applied as appropriate. Fisher's exact and Chi-squared tests were also used. The relationships of colour and dilatation scores with time for the two groups were assessed using regression analysis.

Results

The two groups of children were comparable in age, weight and length of time of application of ointments, with differences not statistically significant. The basic statistics are given in Table 1 and the 95% confidence intervals for the differences between means of the two groups are (−1.2, 0.4) years, (−5.8, 1.6) kg and (−22.1, 22.4) minutes respectively. These intervals provide some information, even though the differences are not significant, since they indicate probable ranges of values with which differences may be compared.

Colour. The elementary statistics for colour and dilatation measurements and their distributional properties are given in Table 2. The differences between EMLA–GTN and EMLA-placebo scores for colour are not significant at the 5% level ($p = 0.20$). The Wilcoxon 95% confidence

Table 1. Elementary statistics for demographic data and time of application of ointments and their distributional properties for the main and EMLA-only groups of children.

Variable	n	Range	$\bar{x}$	SD	95% confidence interval for $\bar{x}$	Chi-squared test for normality
Age; years						
Main group	104	2.3–10.8	6.5	2.1	(6.1, 6.9)	$p = 0.33$
EMLA-only	30	3.0–10.9	6.9	2.0	(6.1, 7.6)	$p = 0.99$
Weight; kg						
Main group	104	13–39	23.4	6.2	(22.3, 24.5)	$p = 0.24$
EMLA-only	30	14–54	25.5	9.3	(22.0, 28.9)	$p = 0.25$
Time of application of ointments; minutes						
Main group	104	50–325	156.8	52.4	(146.6, 167.0)	$p = 0.64$
EMLA-only	30	50–270	156.7	60.7	(134.0, 179.4)	$p = 0.99$

Table 2. Elementary statistics for distributional properties for the EMLA–GTN, EMLA–placebo and EMLA-only measurements for colour and dilatation.

	n	Median	$\bar{x}$	SD	95% confidence interval for $\bar{x}$	Chi-squared test for normality
Colour measurements						
1. EMLA–GTN	104	40.0	37.9	19.5	(34.1, 41.7)	$p = 0.40$
2. EMLA–placebo	104	37.5	36.0	18.2	(32.5, 39.6)	$p = 0.24$
3. EMLA-only	60	23.0	30.3	27.0	(23.3, 37.3)	$p = 0.25$
Dilatation measurements						
1. EMLA–GTN	104	73.0	70.4	24.3	(65.7, 75.2)	$p = 0.14$
2. EMLA–placebo	104	63.5	62.1	27.6	(56.7, 67.4)	$p = 0.053$
3. EMLA-only	60	42.5	42.7	35.1	(33.6, 51.8)	$p = 0.17$

interval for the median of the differences of the two related scores is −0.5, 4.5. Similarly, the differences between EMLA-placebo and EMLA-only scores for colour are not significant ($p = 0.15$), with a 95% confidence interval for the difference between means of −2.0 and 13.6. The colour scores for EMLA–GTN are significantly higher than the scores for EMLA-only ($p < 0.05$) and the 95% confidence interval for the difference between means is 1.0–14.2.

Venous dilatation. The venous dilatation scores for the EMLA–GTN group were very significantly higher than those for the EMLA–placebo group ($p < 0.001$) and for the EMLA-only group ($p < 0.001$). The corresponding 95% confidence intervals for the differences were (3.0, 14.0) (Wilcoxon) and (17.6, 37.9) respectively. Furthermore, the venous dilatation scores for the EMLA–placebo group were very significantly higher than those for the EMLA-only group ($p < 0.001$) and the difference between means had a 95% confidence interval of 8.9–29.8.

Choice of cannulation site. The choice of site was determined more by vein dilatation than skin colour in 86 cases (83%) and by skin colour than vein dilatation in 18 cases (17%) for the main group. The figures for the EMLA-only group were 23 (77%) and 7 (23%) respectively. The differences for each group were highly significant ($p < 0.001$), as were the differences for the two groups combined ($p < 0.001$). The 95% confidence intervals for the larger proportions in the three cases were 0.76, 0.90, 0.62, 0.92 and (0.74, 0.88) respectively, (EMLA-only group: left hand chosen = 15: right hand chosen = 15). The EMLA–GTN site was chosen more often than the EMLA–placebo site. This was a highly significant difference ($p < 0.001$) (Table 3(iii)) and the 95% confidence interval for the difference between proportions of cases was 0.46–0.62.

Ease of cannulation and number of attempts. Table 3(i) also shows that the ease of cannulation is significantly related to the type of ointment used; EMLA–GTN was the easiest, EMLA–placebo moderate, and EMLA-only the most difficult ($p < 0.001$) (Fig. 2). The 95% confidence interval for the difference between the proportions of cases of the first and third groups that were easy to cannulate was (0.22, 0.56). Similarly, the number of attempts at cannulation was significantly related to the type of ointment used. The EMLA-only group required more attempts than the EMLA–GTN group ($p < 0.01$) (Table 3(ii)); a 95% confidence interval for the difference between the proportions of cases that needed a single attempt only was 0.06–0.44.

Regression of measurements on time. Scatter plots showed considerable variation over time for each of the six measurements of colour and dilatation for GTN, placebo and EMLA only, with little discernible pattern in any of the plots. Formal regression analyses confirmed that none of the relationships, between measurements and time, were statistically significant.

Side effects. There were no reported episodes of headache or untoward hypotension.

Discussion

GTN relaxes vascular smooth muscle by the action of its active moiety, nitric oxide, on soluble guanylate cyclase which triggers the formation of endothelium-derived

Table 3. Testing for the significance of the relationships between the type of ointment used and the ease of cannulation, number of attempts needed and the choice of site cannulation. Figures in brackets are column percentages.

		Type of ointment			
		EMLA–GTN	EMLA–placebo	EMLA-only	Significance
(i)	*Ease of cannulation*				
	Easy	42 (66)	19 (37)	14 (27)	Chi-squared = 38.1 df = 4
	Moderate	16 (25)	21 (41)	9 (18)	$p < 0.001$
	Difficult	6 (9)	11 (22)	28 (55)	
(ii)	*Number of attempts*				
	1 Attempt	52 (88)	41 (93)	19 (63)	Chi-squared = 13.2 df = 2
	2 Attempts	7 (12)	1 (2)	4 (13)	$p < 0.01$
	3 or more attempts	0 (0)	2 (5)	7 (23)	
(iii)	*Choice of site*				
	Chosen	79 (76)	25 (24)		Chi-squared = 56.1 df = 1
	Not chosen	25 (24)	79 (76)		$p < 0.001$

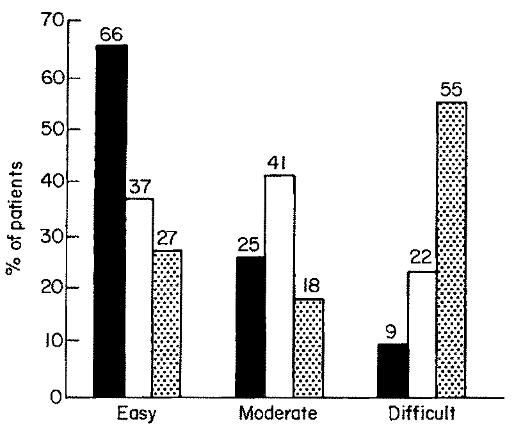

Fig. 2. Graph showing ease of cannulation scores as percentages for EMLA–GTN ■, EMLA–placebo □ and EMLA-only ▩.

relaxing factor (EDRF).[12] Past studies have demonstrated that no significant modification of haemodynamic status (heart rate, right and left ventricular pressures and pulmonary artery pressure) was observed 30 minutes after application of GTN ointment 0.08 mg/kg.[9] This is a higher dose than our 0.8 mg per child. Proprietary GTN patches have been used distal to veins to prolong patency of cannulated veins. The cause of initial skin blanching with EMLA cream appears to be vasoconstriction, as demonstrated by reflectance spectrophotometry and laser Doppler flowmetry; other creams under occlusion also cause blanching. Opacity changes because of oil–water permeation have been refuted. There is a biphasic vasoconstriction–dilatation response to EMLA cream alone.[11] Our study has shown that the addition of topical GTN to the standard EMLA treatment positively affects the choice of site for venous cannulation, when compared with placebo ointment. The choice of site appears to be more dependent on venous dilatation than on colour. The skin colour change counteracting that of EMLA was only demonstrable when comparing the EMLA–GTN group with the EMLA-only group.

There is a significant relationship between vasodilatation and the use of GTN with EMLA. This response was most marked at the site of skin application and to a lesser degree when applied elsewhere on the body. This was observed at the EMLA–placebo sites which were more dilated than the EMLA-only sites.

Previous studies of GTN only have shown no significant effect on ease of cannulation in children aged more than 1 year, but there was demonstrable vasodilatation with locally applied GTN in younger children.[8] The same study concluded that GTN ointment applied elsewhere on the body had no significant effect on the ease of cannulation of veins in children.

Our study was on children older than 1 year. There was a positive effect on ease of cannulation on the EMLA–placebo hands when compared with EMLA-only hands. This could be because application of GTN ointment on the contralateral hand (EMLA–GTN) had an effect on the test site. GTN ointment applied elsewhere on the body has an effect, albeit lesser, on vasodilatation and ease of cannulation.

A recent study comparing pain scores and ease of cannulation in adults randomised into four groups (EMLA–GTN, EMLA–placebo, EMLA only and GTN only) concluded that there were no significant differences in both pain scores and ease of cannulation between the EMLA–GTN group and the EMLA-only group.[19] We have shown in this study a difference in ease of cannulation between EMLA–GTN treated hands and EMLA-only treated hands in children. This could be explained by the more reactive vein of the child.[8]

We conclude that topical GTN ointment and EMLA cream aid venous cannulation in children. Topical GTN ointment affects venous dilatation more than colour of EMLA-treated skin, but the choice of cannulation site depends more on venous dilatation than skin colour.

Acknowledgments

We thank our anaesthetist colleagues and the Pharmacy Department, Ysbyty Gwynedd, for their cooperation during this trial. This project was supported by Gwynedd Health Authority Research Committee. Percutol GTN ointment was supplied by Rorer Health Care Limited. We thank Mr M. J. Kassab for computing help and Mrs M. M. Price for typing the manuscript. This study was presented in part at the North Wales Anaesthetic Forum March 1990 and the Society of Anaesthetists of Wales Spring Meeting March 1990.

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Anaesthesia, 1991, Volume 46, pages 885–901

Correspondence

Consent to clinical research

Dr P.A.J. Hardy (*Anaesthesia* 1990; **45:** 1088) is absolutely correct when he questions the competence of a patient to consent to research during clinical anaesthesia and emphasises the importance of a stringent ethical review.

A case in point is the recent article by Whirley-Diaz and colleagues (*Anaesthesia* 1991; **46:** 220–3). A total of 152 patients, all ASA 2 to 4 were given an anaesthetic which was maintained at 1 MAC and which at no time was designed to include an opioid until well after tracheal intubation and commencement of surgery, and then only if the patients did not respond to a beta-blocker first. We are given no information as to the pre-operative condition of these patients that caused them to be classified as ASA 2 to 4 and whether any of them were receiving any medication

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which might affect the sympatho-adrenal responses. Were any patients at risk from myocardial ischaemia? This information is vital given the authors' defence for maintaining such a light anaesthetic, *viz.* that less than one third of their patients developed tachycardia with this technique. While we are told that the average time from intubation and start of isoflurane to administration of study drug was 34 minutes, we are not told how many patients responded to tracheal intubation either by movement or by increasing their heart rates. This is important because the authors later state in the discussion that the purpose of the study was to report on the effect of esmolol on tachycardia many minutes after intubation. No evidence was presented that if a postintubation response did occur, the pulse and blood pressure were allowed to return to baseline. Such a response would conceivably take a long time to settle, especially when a patient is receiving a 1 MAC anaesthetic. One is left to draw one's own conclusions as to why the authors did not see it fit to measure/report blood loss, seeing that the 'tachycardia frequently occurred well after incision'. One could go on pointing out such omissions and inconsistencies but we are afraid that the only safe conclusion to be drawn from this study is that esmolol is a good beta-blocker and that it effectively masks the signs of light anaesthesia. Incidentally, it would have been interesting to know how many patients in the esmolol groups were then given opioids at the end of the study period.

One cannot but agree with Dr Hardy that we need to review urgently the entire concept of eithically acceptable standards in anaesthesia should we wish to avoid compulsory eithical review of clinical anaesthetic practice. Until such time as we have universally acceptable guidelines and safeguards, our ethical reviews need to be stringent and journals such as *Anaesthesia* have a significant role in ensuring this.

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B. Kaul
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A reply

We appreciate the comments of Drs Kaul and Cork, their genuine interest and thank them for their concern about our patients' competence to consent to research. We assure them that our investigation was examined thoroughly by our Human Investigations Subcommittee and approved by our hospital's Internal Review Board. Further, every patient who was thoroughly competent had the study explained and gave written informed consent. We are extremely confused, however, since it appears that Drs Kaul and Cork then change course and criticise our methodology. The fact that an anaesthetic does not include an opioid does not mean it is ineffective or 'light'. Each patient was premedicated with midazolam and then had thiopentone, N_2O and isoflurane which together comprise a perfectly adequate combination; if necessary, further intervention was included in the protocol as noted. Most of our patients (90%) were ASA 2, they were not cardiac patients and none encountered myocardial ischaemia. If tachycardia occurred, it was only because of surgical dissection, retraction, bone manipulation, drilling, etc.

What is the difference as to how many patients responded to tracheal intubation? At that time none moved, all experienced an increase in heart rate which decreased within 5–15 minutes to control levels. However, this was a study of *surgically* induced tachycardia (average time 34 minutes) after intubation, as the title states. Blood loss was minimal. We are disappointed that Drs Kaul and Cork 'are afraid that the only safe conclusion — is that esmolol is a good beta blocker and — if it effectively masks the signs of light anaesthesia'. We do consider that our patients were adequately anaesthetised and that a sudden extraordinary surgical stimulus occurred which had to be treated. This was a clinical investigation. We believe that our conclusions were reasonable within the framework of the methodology; we believe our own stated four criticisms are acceptable; and finally, that the peer review system of the journal *Anaesthesia* is strict enough to satisfy the most despondent/agnostic reader. Apparently, Drs Kaul and Cork do not fall into this category. We do, finally, recommend as a result of this investigation, that bolus esmolol be given intravenously if unacceptable trachycardia due to surgical stimulation occurs during surgery and anaesthesia.

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Dried blood does not affect pulse oximetry

Pulse oximeter accuracy has been shown to be affected by various factors such as intravenous dyes (particularly methylene blue),[1,2] some nail varnish,[3,4] and some poster paints.[5] Trauma patients may have significant quantities of dried blood remaining on their hands on arrival in the emergency department and, in our experience, there is often insufficient time to clean the patient's hand thoroughly before the application of the pulse oximeter probe. We felt that it was pertinent to investigate whether dried blood on the fingers might also interfere with pulse oximetry.

The finger probes of six commercially available pulse oximeters were applied to the fingers of a healthy male Caucasian volunteer. Two of the fingers had previously been coated in whole blood which was allowed to dry. The saturation given by each oximeter was recorded while the volunteer remained seated and breathed room air. The probes were then rotated between the fingers, so that each probe was applied to each finger in sequence. The saturation readings obtained were noted and the range of saturations recorded for each instrument (Table 1). There was no significant difference in saturation range between those fingers with or without dried blood. The variation between machines was of the same order as between fingers.

It is concluded that, in the emergency situation, the presence of dried blood will not adversely affect pulse

Table 1.

Oximeter	Saturation range (All fingers)	Saturation range (Contaminated fingers)
Datex Satlite	96–97	97
MiniOX IV	96–98	97–98
Kontron 7840	95–98	97–98
Novametrix 515A	96–97	97
Ohmeda Biox 3700	95–96	96
SiMed S-100	96–98	98

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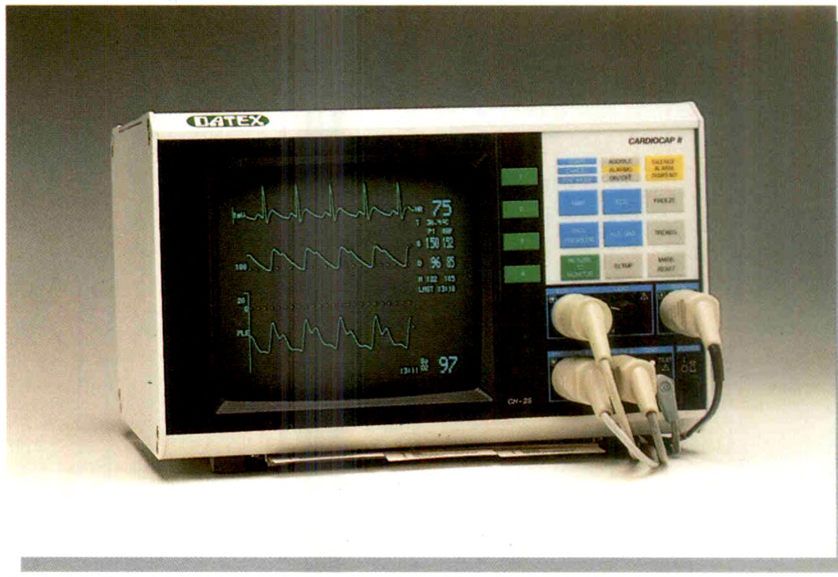

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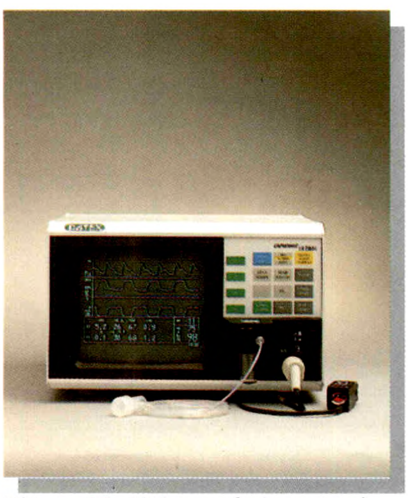

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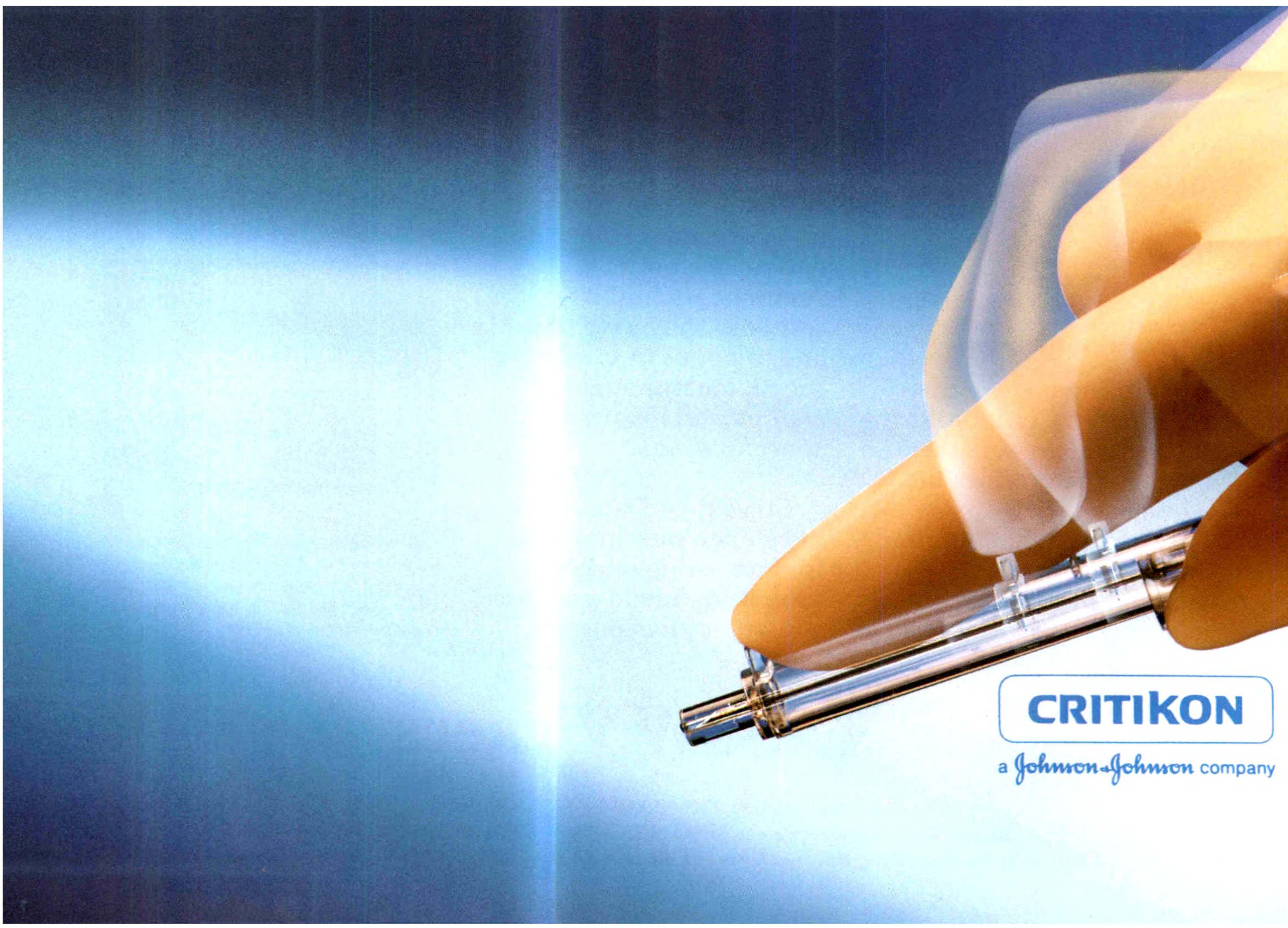
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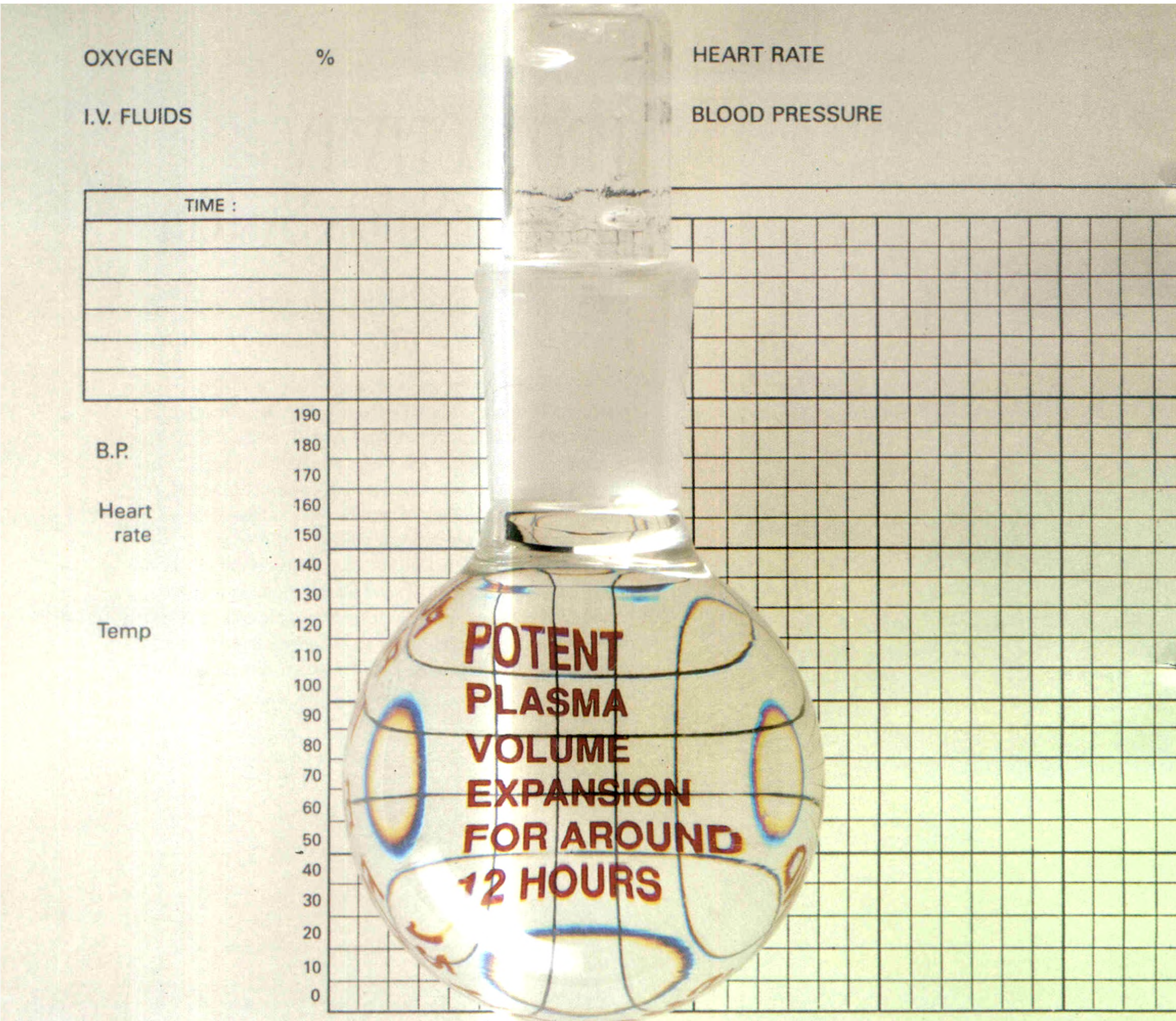

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Pulse oximeters and poor perfusion

Professor Runciman and his colleagues (*Anaesthesia* 1991; **46:** 3) are to be congratulated on their detailed study of a large number of pulse oximeters. However, we are concerned that the publication of a 'league table', ranking different instruments in a particular order, may be misleading to potential purchasers.

When peripheral perfusion is reduced the pulse wave amplitude diminishes and its shape resembles a sine wave rather than the characteristic rapid upstroke and exponential decay with a dichrotic notch. Pulse oximeters generally make multiple measurements of transmitted red and infrared light every second and compare one with another in order to determine if any change is due to arterial pulsation or to artefact. Both the amplitude and the shape of the waveform are important in discriminating pulse from artefact. Resulting measurements of Sp_{O_2} are weighted, fed into an algorithm and the resulting average displayed on the front panel. Different manufacturers use different strategems when the changes in light transmission as a result of arterial pulsation approaches those caused by artefact. Some calculate internal 'confidence intervals' and warn the user that the displayed value may not be reliable. Others stop displaying a value and search for a pulse wave while some hold the last value while searching for the pulse wave. The former two methods are clinically acceptable as the user should not be given unreliable data provided that the manufacturer has set the level appropriately. The dilemma for the manufacturer is that if he errs on the side of safety and indicates a problem with signal strength before his competitors, he runs the risk of being accused of inadequate performance under conditions of poor perfusion. The converse situation, where an instrument continues to display a value when pulse amplitude is too small for reliable data collection, is dangerous clinically, but likely to win approval in poorly designed studies of poor perfusion where oxygenation is normal and unchanging.

The only acceptable method of checking proper pulse oximeter function is to examine the response to *changes* in oxygenation. Our own studies,[1-3] which have examined a number of different aspects of pulse oximeter function, have been conducted in volunteers and have included intermittent exposure to hypoxic gas mixtures. Such studies test the most important purpose of pulse oximeters, namely their ability to detect the sudden onset of hypoxaemia. Our 'league table' of pulse oximeters would look very different to that of Professor Runciman.

The most recent study from this Department[3] has shown the ability of motion artefact to induce changes in the displayed Sp_{O_2} and delayed detection of hypoxaemia. Shivering is a common occurrence in the rewarming period following cardiopulmonary bypass and we feel that it is possible that some of the changes seen by Professor Runciman's group might have been due to motion artefact.

The choice of a pulse oximeter is important and comparative studies are essential. Potential purchasers should be cautioned that accuracy and precision are not sufficient criteria for a decision and the ability to detect hypoxaemia reliably under adverse conditions should be considered.

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Contamination of piped oxygen supplies

We wish to report a most disturbing incident which occurred at our hospital recently. During the course of a routine neurosurgical operating list, the inspired oxygen concentration being delivered to two patients in adjacent operating theatres was seen to decrease to below 20% simultaneously. Both patients were, at the time, receiving gas mixtures set to contain 33% oxygen. One ventilated patient suffered a transient drop in oxygen saturation to below 90%. The analysed oxygen concentration to both patients recovered promptly on switching over to the anaesthetic machine cylinder supply.

A warning was passed to the neurosurgical intensive care unit (ICU), in the same building, that there might be a problem with the oxygen supplies, and a Datex 'Capnomac' multigas analyser was attached to one of the wall outlets. Initially, this indicated that the gas being supplied was 100% oxygen, but about 20 minutes after the initial incident in the operating theatres there was a rapid decrease to 22% oxygen. One patient suffered a decrease in oxygen saturation to 88% for a period of 1–2 minutes before the backup oxygen cylinder could be plugged into the ventilator. Transferring all the ventilators to their backup cylinders took 4–5 minutes and, on returning to the analyser at the end of this period, it was noticed that the display was again reading 100%.

With the certainty that there had been an unknown

contaminant gas in the piped oxygen system, the entire site was transferred onto cylinder supplies whilst an investigation into the cause of the problem was carried out. All routine operating in the main theatre suite was cancelled, since the great majority of the anaesthetic machines had provision for only one oxygen cylinder. Sampling from the operating theatres and ICU carried out by a quality control pharmacist detected no contamination. Further sampling at the liquid oxygen VIE, at the reserve cylinder bank and at other points in the hospital proved similarly negative. Pressure tests conducted on the ICU however, discovered that the medical air supply was at a significantly higher (3 PSIG./20 KPa) pressure than the oxygen supply.

A small amount of the contaminant gas had been trapped in one of the operating theatre anaesthetic machines which was shut down during the initial incident; later analysis by mass spectrometry produced the following results: oxygen 82%; nitrous oxide 8%; argon 0.3%; nitrogen 9%; halothane 1%. These figures are highly suggestive of contamination of the system with air, as later significant contamination of the sample with atmospheric air would have diluted the halothane vapour (the vaporizer had been set to 1%). The investigation therefore concentrated on finding a plausible route of entry into the system for compressed air.

Given the established pressure differential on the ICU, it would be feasible for reverse flow to occur through a faulty piece of equipment such as an oxygen/air blender and there are precedents for this.[1] However, after testing all such equipment which had been in service at the time of the incident, no conditions could be produced under which reverse flow occurred. During the period in which the incident occurred, work had been in progress on the oxygen pipework on one of the wards. A Permit to Work was issued to cover this, but it had not been signed by a doctor. The work included a pressure test of all the ward pipework with compressed air at 8 Bar, as outlined in the HTM22 regulations. However, the regulations also state that the lines under test must be physically isolated by removal of a length of pipe before testing can take place. The engineering department has assured us that this precaution had been taken. The question of whether any air from the ward could have reached the neurosurgical building and produced the required pattern of contamination is difficult to answer in view of the complexity of the system as a whole.

After 48 hours, during which the whole system was flushed, all outlets checked for faulty equipment and the medical air pressure to the ITU adjusted to be below that of the oxygen, the pipelines were declared safe for use again. The problem has not recurred. A definite cause has not been located, but the episode underlines the advantages of continuous gas monitoring both in operating theatres and in Intensive Care Units. All present central monitoring systems rely on pressure faults to sound an alarm and could not have detected this problem. A second point involves provision of adequate reserve oxygen on the machine to allow the safe continuance of a case in the event of a piped supply failure. Finally, the events also show that a working understanding of the systems which deliver gas to the clinical areas can be an advantage to the anaesthetist when problems occur and that one should not assume that one's knowledge only need extend as far as the socket on the wall.

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I.F.M. GRAHAM
S.L. SNOWDON

Reference

1. DHSS. Health Services Management Hazard Notice No. (81) 4: Failure of Medianda Oxygen/Air mixer unit.

Evaluation of heat and moisture exchangers

There is a need for data on heat and moisture exchangers (HMEs) to guide clinical practice on their use in the care of children. The recently published method employed to determine the resistance of one such HME, the Portex Thermovent 600 (*Anaesthesia* 1991; **46:** 296–9) must, however, be questioned. The absence of data on the moisture conserving properties of the device, perhaps a key indicator of the acceptability of HMEs in clinical use, was also noteworthy.

The method used to measure the resistance, as employed by Buckley,[1] appears to me to be inappropriate. Buckley placed a Pall Ultipor BB50 filter in the inspiratory limb of a breathing system, between a heated humidifier and the patient, to prevent organisms from the ventilator and humidifier infecting the patient. However, condensation collected in the filter as a result of the hydrophobic nature of the Pall filter and caused an increase in resistance. The Thermovent 600 is solely, however, a hygroscopic HME and so there are no claims concerning the prevention of the passage of organisms through it. In consequence it would never be used in the location in which these authors tested it. It would be more relevant to place the Thermovent 600 at the patient connection port, as in normal clinical use, and subject it to a period of ventilation for, say, 24 hours. With this test arrangement it would be possible to determine whether the HME is likely to become heavily laden with excess water in normal clinical use, and whether it would be necessary to remove an arbitrary amount of the excess water before the resistance was determined. This suggested test arrangement would also allow an indication of the moisture conserving performance of the HME to be made.

We evaluate HMEs for the Department of Health as part of the *Evaluation* series of publications. We have found it difficult to measure the pressure difference across a wet HME because of the drying effect of the flow of air. Nevertheless, there is only a small increase in resistance across this type of HME when it becomes wet. As a physicist who does laboratory tests of HMEs and not a clinician, I cannot, of course, comment on their clinical value, a question which must be answered by others.

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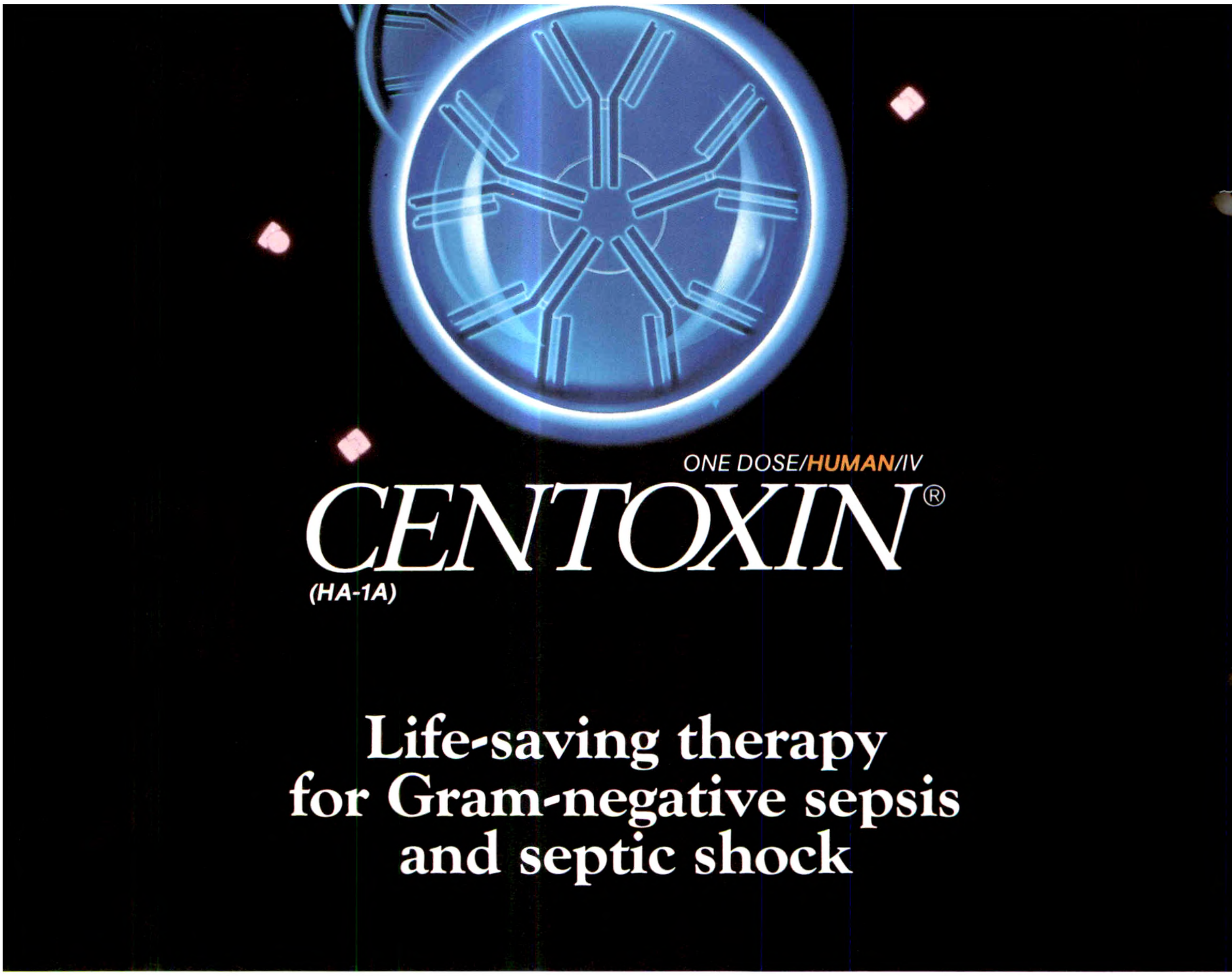
References

1. BUCKLEY PM. Increase in resistance of in-line breathing filters in humidified air. *British Journal of Anaesthesia* 1984; **56:** 637–643.

A reply

Thank you for the opportunity to reply to Mr Wilkes' letter.

In answer to concerns raised as to the efficacy and suitability of the method used to saturate the HME, we



ABBREVIATED PRESCRIBING INFORMATION

PRESENTATION Centoxin is a solution for intravenous infusion after dilution with normal saline. Each vial contains: HA-1A 100 mg/20 ml

USES Centoxin is indicated for the treatment of patients with the sepsis syndrome and a presumptive diagnosis of Gram-negative bacteraemia, especially those with septic shock. Centoxin therapy should be given in hospital, along with the appropriate antibiotics and supportive therapy, as soon as Gram-negative sepsis is clinically suspected. Centoxin should be given once and is not intended for repeated use.

DOSAGE AND ADMINISTRATION The recommended dose of Centoxin is a single 100 mg intravenous infusion. Centoxin should be administered intravenously over a period of 15 to 30 minutes in a total volume of 70 mL after dilution with normal saline for injection. In patients studied to date, it has not been necessary to adjust the dosage for renal or hepatic function.

CONTRA-INDICATIONS, WARNINGS ETC. Contra-indications Centoxin should not be used in patients whose primary injury involves burns, since no studies have been done in those patients. Centoxin should not be used in patients with known hypersensitivity to murine proteins. Centoxin should not be used in patients with previous exposure to HA-1A. **Undesirable Effects** No serious or life-threatening adverse reactions attributable to Centoxin were reported among the more than 300 patients who received the product in clinical trials, including more than 45 patients who received 200 or 300 mg of HA-1A as a single dose. Transient flushing, localized urticaria and hypotension have been reported rarely (<1%) in patients receiving Centoxin. Human antibodies against Centoxin have not been detected. **Special Precautions** *In vitro* and *in vivo* mutagenicity studies have not demonstrated any mutagenic effect. Studies have not been performed to evaluate the carcinogenic potential or effects on fertility in male or female animals. The use of Centoxin in children has not been extensively studied. Centoxin has been administered to a small group of children (ages 10 months to 13 years), the majority of whom had fulminant meningococcaemia with shock and purpura. The dose administered was up to 6 mg/kg to a maximal dose of 100 mg. Centoxin was well tolerated by all patients. The efficacy of Centoxin in adults and children with meningococcal septicaemia has not been established and therefore the use of Centoxin in meningococcal septicaemia cannot be recommended. Centoxin contains a murine J chain, which suggests that anti-HA-1A

CENTOXIN: The first human monoclonal antibody specifically directed against endotoxin

Centoxin (HA-1A) is a human monoclonal IgM antibody targeted against endotoxin – the substance largely responsible for multiple organ failure and death associated with Gram-negative sepsis and septic shock. Centoxin neutralizes the lethal effects of endotoxin and helps save the lives of septic patients.

Early and sustained reductions in mortality in Gram-negative sepsis and septic shock

In a multicentre, double-blind, placebo-controlled trial, Centoxin was administered to septic patients with presumptive Gram-negative bacteraemia, including those with septic shock. Clinical results demonstrate significant early and sustained reductions in mortality in septic patients with Gram-negative bacteraemia, especially those with septic shock.[1]

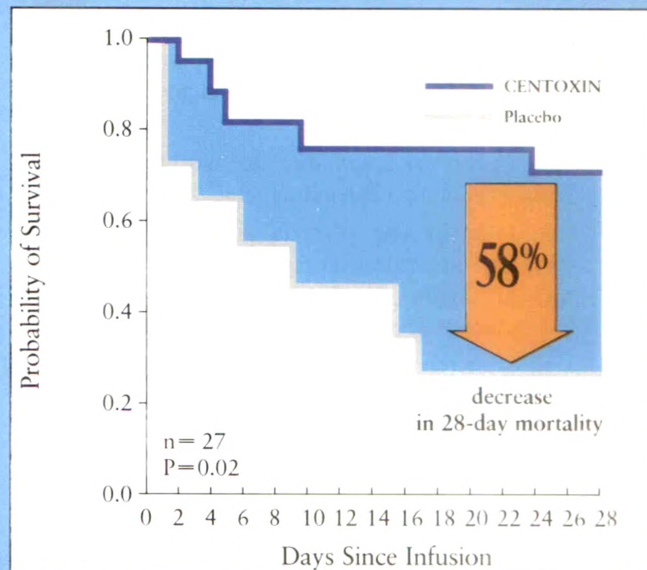
Reduction in 28-day mortality[1]

	Mortality			
Population	Placebo*	Centoxin	% Reduction	*P* Value
Gram-Negative Bacteraemia (N=200)	49% (45/92)	30% (32/105)	39%	0.014
Gram-Negative Bacteraemia with Shock (N=102)	57% (27/47)	33% (18/54)	42%	0.017

*Three placebo-group patients (one with shock) were discharged from the hospital and lost to follow-up before day 28.

58% decrease in mortality in endotoxaemic patients[2]

Centoxin decreased mortality in endotoxaemic patients – patients in whom a human anti-endotoxin monoclonal antibody should work best.



Centoxin:

- Effective in significantly reducing mortality in both severely ill and less severely ill patients with:
  - shock and without shock[1]
  - high APACHE II scores (>25) and low APACHE II scores (≤25)[1]
- Safe and nonimmunogenic in clinical studies conducted to date[1,3]
- Administered in a single fixed dose regardless of disease severity, renal and hepatic function

ONE DOSE/**HUMAN**/IV

CENTOXIN®▼

(HA-1A)

Saving lives in Gram-negative sepsis and septic shock

antibody formation is a possibility. Nevertheless, in clinical trials, anti-HA-1A antibodies were not detected (with a radioimmunoassay) in blood samples taken from patients up to 35 days after administration of a single dose of Centoxin. The immunogenic risk of repeated administration of Centoxin has not been extensively investigated. **Use During Pregnancy and Lactation** There has been no experience to date with the use of Centoxin in pregnant patients, and animal reproduction studies have not been conducted. Therefore, Centoxin should be used in pregnant patients only when, in the judgement of the physician, anticipated benefits outweigh the potential risks. It is not known if Centoxin is excreted in human milk. **Interaction with Other Medicaments and Other Forms of Interaction** There have been no reports of interactions between Centoxin and other drugs used concomitantly in the treatment of Gram-negative sepsis. **Overdose** The maximum amount of Centoxin that can safely be administered has not been determined. However, single doses as high as 300 mg of Centoxin have been safely administered to adults, and doses of 6 mg/kg up to a maximum of 100 mg to children from 10 months to 13 years of age. **Effects on Ability to Drive and Use Machines** HA-1A is pharmacologically inert and can therefore not be expected to affect the ability to drive and use machines. It is, in any case, administered only to hospitalized, seriously ill patients.

LEGAL CATEGORY POM.
PACKAGE QUANTITIES Centoxin is available as a package containing 1 single dose 20 ml vial. **Product licence number** 8563/0010 **Basic NHS cost** £2,200. **Date of preparation** May 1991. For further information refer to data sheet or contact: Centocor Medical Services, Centocor B.V., Einsteinweg 101, 2333 CB Leiden, The Netherlands Tel. 0800-898458 A 2001

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Centocor®
Centocor B.V., Leiden, The Netherlands.

chose a method most likely, in our opinion, to provide full saturation of the gas delivered. Concerns about the suitability of methods used in the preparation of HEI 166,[1] prompted us to adopt a technique which might ensure this. We would tend to concur with Bethune[2] with regard to the necessity of providing saturated gas when simulating expiratory flow from the patient. We in no sense recommend the use of the test circuit arrangement in clinical practice (as clearly stated in our paper). However, we feel that its use in an attempt to subject the device to maximal humidity was justified, particularly with respect to subsequent resistance measurements.

Buckley's work on the Pall Ultipor BB50,[3] a device which has been used as an in line filter and as an HME,[1] aimed to investigate potential problems of placing such respiratory equipment in both the inspiratory (distal to a heated water bath humidifier) and expiratory limb of the breathing system. The increase in resistance that occurred in the system was a direct result of the amount of condensation that resulted. The arrangement used by Buckley, although intended to represent the optimal positions to provide patient protection from bacterial contamination, was not dissimilar from that chosen by previous workers investigating the physical characteristics of HMEs.[4] Our investigations of the device yielded comparable results to those workers independently examining very similar devices, but using other test and measurement techniques.[1,5]

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A modified technique for the insertion of an interpleural catheter

Since the technique of interpleural analgesia was described by Reiestad and Stromskag,[1] it has gained popularity for pain relief after cholecystectomy, mastectomy, and renal operations.

The introduction of air into the interpleural space is difficult to avoid as the epidural needle is opened to air to allow passage of the catheter. A frequency of pneumothorax of 2% has been reported,[2] and about 10–20 ml of air is normally sucked into the pleural space during catheter placement. These pockets of air may be responsible for the patchy blocks sometimes encountered with this technique. We have devised a technique which prevents the interpleural space ever being open to atmosphere. The equipment used for this technique is readily available and consists of a Tuohy needle, three-way tap, 2 ml syringe and an epidural catheter.

With the patient in the lateral position, a 16 gauge Tuohy needle is advanced to make contact with the fifth rib and the stylet is removed. A 2 ml syringe joined to a 3-way tap, primed with normal saline, is connected to the epidural needle and the plunger of the syringe removed. The epidural needle is then advanced in the usual manner until the fluid level suddently drops as a result of the negative pressure within the thorax during inspiration, identifying the interpleural space. The 3-way tap is now turned off to the patient and the catheter threaded through the fluid level and the 2 ml syringe (Fig. 1). The tap is now opened and the catheter passed through the epidural needle and 5–6 cm into the interpleural space. Once the catheter is within the epidural needle there is very little further fall in the fluid level, and this acts as a seal preventing air entering into the interpleural space. The Tuohy needle can then be removed in the usual way. In our experience the technique is easily performed.

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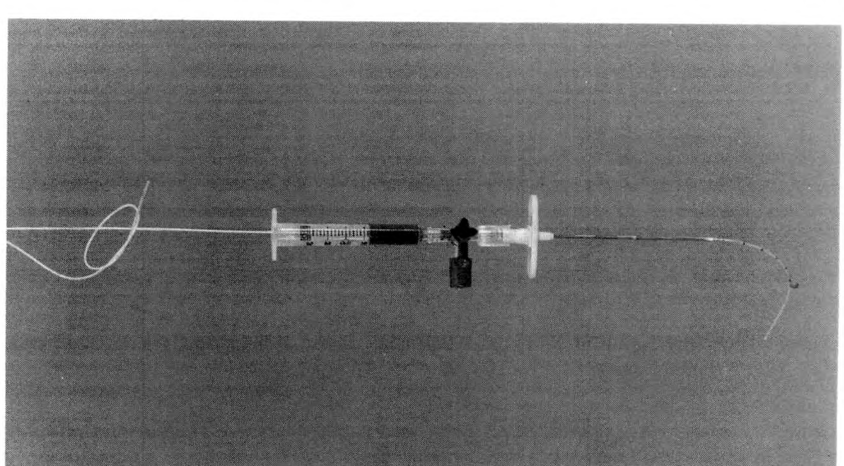

Fig. 1.

Leaking T-connector in Toptronic oxygen analyser

Leaks in various components of anaesthetic breathing systems are a well recognised cause of hypoventilation. During a block dissection of neck, a Toptronic oxygen analyser, model 74223, was sited at the outlet of the Boyle's machine upstream from a Manley Pulmovent minute volume divider ventilator. The ventilator was observed to cycle more slowly than normal for the selected gas flows and a check of the system revealed a silent leak from the T-connector of the oxygen analyser that allows sampling of the fresh gas flow by the fuel cell. Here there is a screw-in connexion, sealed with an O-ring, which, although not obviously loose, was the source of the leak (Fig. 1). The oxygen analyser was immediately removed from the circuit and when dismantled, the O-ring appeared normal and undamaged. The degree of leak was found to vary with the amount of backpressure in the system, and as backpressure is created upstream of the Manley Pulmovent, this increased the degree of leakage. The manufacturers are at present looking into the problem and in the meantime, Toptronic oxygen analysers in this hospital are being additionally sealed with silastoseal. Meanwhile, it would seem sensible to avoid siting this oxygen analyser upstream from a minute volume divider ventilator where significant backpressure increases the risk of leakage. Also demonstrated is the desirability of routine end-tidal carbon dioxide monitoring as a means of detecting leaks of this type at an early stage in patients whose lungs are being mechanically ventilated.

The incident has been reported to the Scottish Home and Health Department as a potential hazard.

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Fig. 1.

Device to maintain the position of spinal needles

Dr Simsa describes an elegant device to maintain the position of a 29-gauge spinal needle when inserted through an epidural needle (*Anaesthesia* 1990; **45:** 593–4). I would like to suggest a simple alternative method based on the use of small bore extension tubing as originally detailed for nerve blocks by Winnie.[1] Its use will prevent displacement of a spinal needle whether inserted through an introducer or an epidural needle.

I use the extension set with 'T' Adaptor (SL no. 898, Abbott Venisystems) which has an internal volume of 0.4 ml (Fig. 1). A syringe is attached to the extension tube and filled with local anaesthetic via a drawing-up needle so

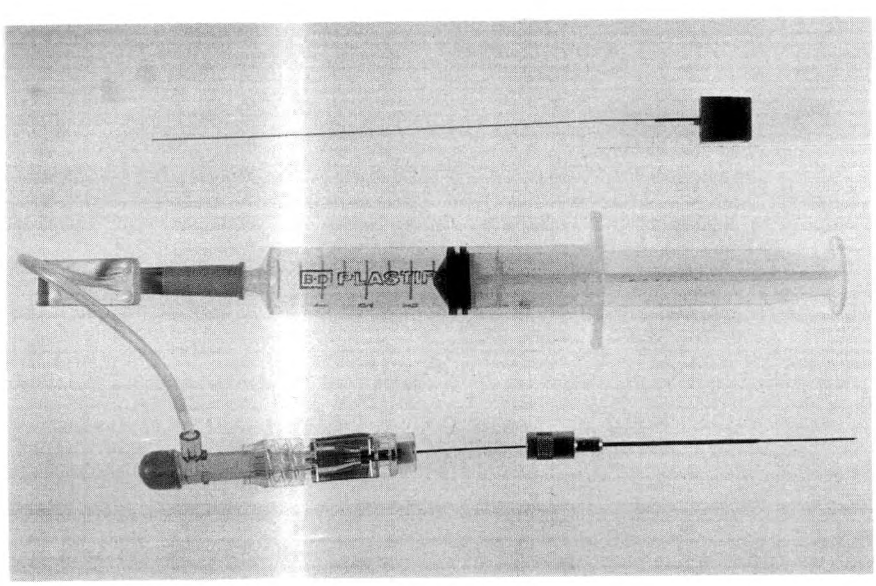

Fig. 1.

that the tube is primed and the syringe contains the volume of local anaesthetic to be injected. Lumbar puncture is performed, after which the extension tubing is attached to the spinal needle. Aspirations and injections can then occur without disturbing the needle because of the flexibility of the tubing. It is important to limit the aspiration volume to less than that of the extension tubing so that CSF does not enter the syringe, which would lead to a small overdosage.

I have used the device with both 26- and 29-gauge needles without difficulty. The cost is small compared with the consequences of inadequate anaesthesia. An even more simple device without the 'T' adaptor and Luer fittings could be incorporated into spinal needle packs for little extra charge.

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The use of the laryngeal mask airway to assist fibreoptic orotracheal intubation

Fibreoptic endoscopic-guided intubation for difficult tracheal intubation has been used in different ways for a number of years.[1,2] The laryngeal mask airway (LMA) has also been used to facilitate difficult intubation.[3] We report a simple technique, recently used, by which the LMA acts as a guide for a fibreoptic laryngoscope. Subsequent placement of an orotracheal tube is then possible. Approval to use this technique was obtained from the chairman of the local ethics committee.

A well lubricated fibreoptic laryngoscope (Olympus LF1) is passed through a rectal tube, the internal diameter of which is 7.3 mm (Warne Surgical Products). After induction of anaesthesia, using fentanyl and propofol, a size 3 LMA is inserted and anaesthesia is deepened and maintained using 30% oxygen in nitrous oxide and halothane, with the patient breathing spontaneously. The LMA is connected as usual to the breathing circuit with a 3-way swivel connector, the internal diameter of which is 9 mm. The fibrescope with the guide tube over it, is passed through the LMA (Fig. 1) and advanced through the vocal cords until the carina is in view. The fibreoptic laryngoscope is then withdrawn leaving the guide tube in the trachea. An 8.5 mm cuffed tracheal tube can then be railroaded over the guide tube and the guide removed. Successful placement of the tracheal tube is confirmed by movement of the breathing bag, auscultation and capnography. Our criterion for safety during the procedure is to maintain oxygen saturation at 97–100%, using appropriate control of the inspired oxygen concentration.

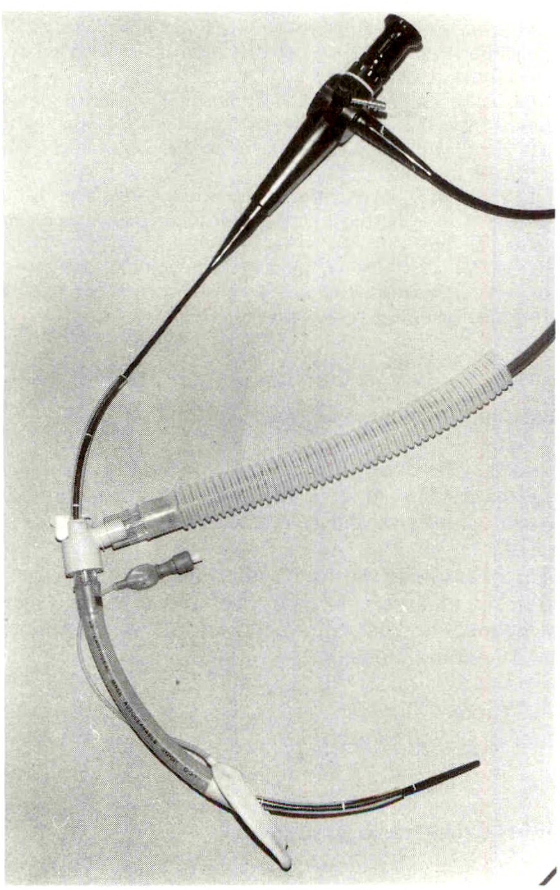

Fig. 1.

The rectal tube is used as a guide over which the LMA may be removed and a large diameter tracheal tube railroaded into the trachea. Without it, only a narrow tracheal tube of sufficient length, perhaps twice the length of the LMA, that will permit removal of the LMA, may be railroaded over the fibreoptic laryngoscope into the trachea. We do not believe that such tubes are available. Although the resistance with the rectal tube *in situ* is high, the tracheal tube is rapidly railroaded over the rectal tube, which is then removed. The technique described allows a margin of safety throughout as at no stage is there irreversible compromise of the airway. Furthermore, the technique is practical even for those anaesthetists with no specific training in fibreoptic intubation, although the bars on the LMA might be mistaken for the vocal cords.

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The use of a 25-gauge Whitacre needle for spinal anaesthesia in orthopaedic surgery

Recent emphasis on the configuration of the needle tip as an important aetiological factor in postspinal headache (PSH) has led to a revival of interest in the use of the Whitacre needle for patients with a high risk of developing PSH following spinal anaesthesia.[1,2] Pencil-point needles have a theoretical advantage in reducing trauma to the dural fibres[2] and recent experimental studies suggest that the dural defect produced by 22-gauge Whitacre pencil

point needles is smaller and leads to a smaller loss of cerebrospinal fluid (CSF) than with comparable Quincke needles.[3] Recent clinical studies demonstrating an incidence of PSH under 4% in younger patients using a Whitacre 22-gauge needle[4] would seem to support these experimental findings.

Up to now, the only commercially available Whitacre needle was the 22-gauge size, until a 25-gauge version became available recently. It is thought that a smaller pencil-point needle should cause less PSH than comparable Quincke type needles and that it could approach the low incidence of PSH associated with extreme fine gauge Quincke needles (e.g. 29 gauge) while retaining the ease of handling of the larger 22 gauge Whitacre needle. We examined these issues in a controlled study of 200 orthopaedic patients (ASA group 1–3) aged 15–84 years undergoing elective orthopaedic procedures who were allocated randomly to receive spinal anaesthesia with either a 22-gauge Whitacre needle (Becton and Dickinson, BD, outer diameter 0.7 mm) or a 25-gauge Whitacre needle (BD outer diameter 0.5 mm). Successful dural punction was achieved in all patients in both groups. The overall incidence of classical postdural puncture headache was 2% in the 25 gauge and 4% in the 22 gauge group and the incidence of nonspinal headache and backache was similar in both groups. No patients required more than two attempts at lumbar puncture.

In the light of these findings, a 2% incidence of PSH with the 25 gauge Whitacre needle is clearly lower than that reported with 25 or 26 gauge Quincke needles[5,6] and approaches results obtained with 29 gauge needles. This low incidence of PSH is even more impressive if the results in patients under 40 years are further analysed, where the PSH incidence in the 22 gauge group was four times higher (5.3% compared with 1.4%). The use of extreme fine-gauge needles (e.g. 29 gauge) gives good results in experienced hands; however, their use is associated with a higher rate of failed spinal anaesthesia than following the use of larger needles.[1] A further theoretical advantage of the 25 gauge Whitacre needle over the 29 gauge needle is the provision of a transparent hub; this makes earlier identification of CSF possible.[2] Although introduction and placement of a Whitacre needle feels very different from that of a Quincke needle,[1] expertise is quickly attained, as testified by the low rate of attempts at spinal anaesthesia in this study. The Whitacre 25 gauge needle is still rigid enough to be used without an introducer, although this may be initially useful for those inexperienced in the use of Whitacre needles.

These results suggest that the use of a 25-gauge Whitacre needle can effectively reduce the incidence of PSH compared to a 22-gauge Whitacre needle, whilst the low failure rate in using this needle would suggest that the ease of handling of the larger Whitacre needle has been retained. It is a suitable choice for spinal anaesthesia in young patients and may be used as an alternative to the 29 gauge needle in this patient group.

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Dental trauma during Entonox inhalation via mouthpiece

Trauma to crowned teeth and replacement dentition is a well recognised complication during general anaesthesia. This is often associated with the use of a rigid oral airway. We wish to describe a similar problem associated with the administration of Entonox for analgesia in labour. A 29-year-old multigravida in advanced labour was having Entonox analgesia via a mouthpiece. During a painful contraction she bit forcibly on the rigid mouthpiece and sheared off an upper second incisor crown. This raises the question of using mouthpieces for Entonox administration during labour in patients with crowns and replacement dentition. Because of patient preference for using mouthpieces instead of a face mask, patients should be advised of this risk and be offered the use of a face mask instead.

The anaesthetist has a responsibility to ensure correct practice in all aspects of pain relief in labour. This applies just as much to the safe administration of Entonox as it does to epidural analgesia.

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C. CALLANDER

Dosage of phenylephrine in spinal anaesthesia for Caesarean section

We would like to express some concerns regarding the preparation of phenylephrine injection which recently appeared in your columns (*Anaesthesia* 1991; **46:** 314–5).

Soft plastic infusion containers, such as 'Steriflex', are only designed for single use, and are not intended to be used for extemporaneous dilutions. For this reason, they are poorly designed for the preparation of very dilute solutions. In addition, they require careful labelling if they are used for this purpose in order to prevent their accidental use as normal infusion solutions, and it should be emphasised that a different syringe should be used for withdrawing a dose from the bag than the one used to dilute the original ampoule. Thorough mixing of drug and diluent by vigorous shaking of the bag is also essential to remove any concentration gradient in the region of the septum. The actual volume of a 'Steriflex' bag of 500 ml 0.9% sodium chloride solution ranges from 500 ml to approximately 560 ml (Baxter Healthcare Ltd, personal communication). This is because the bags are permeable to water vapour and therefore losses are expected during

storage. As a result of this, the concentration resulting from the addition of a 1 ml ampoule containing 10 mg phenylephrine will vary from bag to bag, and from approximately 17 μg/ml to 20 μg/ml. A 2.5 ml bolus dose, for example, could contain anything between 44–50 μg of active drug. While it is accepted that the patient's clinical condition will be used to determine the dose given, we would contend that a potential dose variability of 10% is unacceptable.

The septum of the 'Steriflex' bag is designed for a maximum of 10 punctures by 19 gauge needles, under aseptic conditions. The sterility of a bag punctured repeatedly under nonaseptic conditions cannot be guaranteed.

The diluents for phenylephrine mentioned in the letter are 'saline or similar'. While there are no problems of physical compatibility of phenylephrine with sodium chloride 0.9% and dextrose 5% in water,[1] phenylephrine is potentially incompatible with more alkaline solutions, such as sodium bicarbonate.[2] The preparation and use of the phenylephrine injection as described is not covered by a data sheet/product licence and such use would therefore occur solely under the doctor's own responsibility.

For the reasons stated above, we feel that any phenylephrine dilutions should be prepared under aseptic conditions by a pharmacist. In addition to ensuring the sterility of the finished product and its presentation in appropriate dose volumes, quality control and standard pharmaceutical manufacturing procedures will ensure reproducible and accurate solution strengths. This is obviously extremely important in relation to potent drugs, used at high dilutions.

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A case of patient controlled analgesia exacerbating postoperative pain

An 8-year-old boy presented for a nephro-ureterectomy to remove a functionless kidney. Anaesthesia and surgery were uneventful. During the course of surgery he received 0.2 μg/kg of morphine intravenously. Postoperatively his pain control was provided via a Bard Harvard patient controlled analgesia (PCA) machine, utilising a background infusion of morphine of 20 μg/kg/hour, together with self-administered boluses of 10 μg/kg. Pain control was initially satisfactory. However, on the day following surgery, each bolus began to precipitate an intensification of his abdominal pain, particularly in the epigastric and umbilical areas. The exacerbation of the pain occurred within 5 minutes of each bolus dose. The morphine was therefore discontinued and replaced by a PCA machine containing pethidine. The change in therapy brought the intermittent exacerbations of the pain to a halt and satisfactorily controlled the patient's abdominal pain. Investigations revealed a high serum amylase, which reached a peak of 1798 units. Ultrasound examination of the liver, biliary system and pancreas showed no abnormalities.

Overall it was felt that morphine in the PCA machine had precipitated acute pancreatitis, possibly secondary to spasm of the sphincter of Oddie.[1] This produced the peculiar and rather surprising effect of abdominal pain that was exacerbated by each dose of analgesic requested from the PCA machine. Subsequently all signs of pancreatitis subsided and the patient made a good recovery.

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Reference

1. WAPSHAW H. The pancreatic side effects of morphine. *British Medical Journal* 1953; **1**: 373–5.

Cyclopropane and Datex Capnomac

A recent article (*Anaesthesia* 1991; **46**: 398–9) reported the effect of cyclopropane on the measurement of volatile anaesthetic agents measured with the Datex Capnomac. As mentioned in the article, the Capnomac uses infrared absorption for the measurement of anaesthetic agents. This technique is used in most anaesthesia gas monitors from several manufacturers. The wavelengths used vary between different brands, but most of the monitors, if not all, are affected by cyclopropane.

Capnomac, like all other anaesthesia gas monitors, has been designed to be used for measurement of the most common anaesthetic agents. The use of Capnomac for monitoring highly flammable volatile agents like cyclopropane is strictly forbidden by the manufacturer. A warning of this can be read both from the monitor's rear panel and from its Operator's Manual. Unfortunate as it may be, according to our knowledge, no current manufacturer of anaesthesia gas monitors makes or develops monitors to be used with cyclopropane.

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M. PALOHEIMO

Propofol for sedation of a spontaneously breathing infant

Propofol is well known as an induction agent and for maintenance of anaesthesia by continuous infusion,[1] for sedation of adults during regional anaesthesia and of artificially ventilated patients in the intensive care unit.[2] The use for sedation in children while spontaneously breathing has not been described previously. A 28-month-old, 14.5 kg male infant was admitted to hospital suffering acute respiratory distress due to upper airway obstruction. After induction of anaesthesia with halothane in oxygen, bronchoscopy was performed. A tough plug of mucus was

removed from the subglottic area. Inspection revealed the tracheal mucosa to be swollen and hyperaemic. Xylomethazoline was applied topically and antibiotics and prednisolone administered intravenously. After removal of the bronchoscope, the trachea was intubated orally and he was admitted to intensive care unit. The ECG and pulse oximetry were displayed continuously. Sedation was started with a bolus of midazolam 1 mg intravenously with incremental doses of 0.5 mg to a total of 3.5 mg in 10 minutes. Because the desired effect was not reached, 30 mg propofol (2.1 mg/kg) was administered, followed by a continuous infusion of 3.5 mg/kg/hour. The patient breathed oxygen enriched air ($F\text{IO}_2$ 0.5) via a nebuliser.

Because of the ineffectiveness of midazolam and problems known to exist when it is used by continuous infusion over prolonged periods,[3,4] we decided to continue the use of propofol. Experience with comparable cases in adults has shown that propofol is a suitable drug to be used in this way. The initial dose of propofol (3.5 mg/kg/hour) was small, but produced adequate sedation, probably due to the previous use of midazolam. The infusion rate of propofol was gradually increased and ultimately a mean dose of 8 mg/kg/hour was necessary to maintain adequate sedation. During this time, the arterial blood pressure remained stable and there was no evidence of respiratory depression; oxygen saturation remained at 99%. This dose is lower than the dose needed for maintenance of anaesthesia in children (12–19 mg/kg/hour),[5,6] but is similar to the average dose reported for sedation of a 9-week-old child during artificial ventilation.[7]

We conclude that propofol is a suitable alternative for sedation of children in intensive care.

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Visual disturbances after transurethral resection of the prostate

I disagree with Dr J. N. Cashman's view (*Anaesthesia* 1990; **45:** 69), that transient blindness after TURP was due to glycine-induced oedema of the visual cortex. We have had during the past 6 months four cases of transient blindness varying from 4 to 12 hours, following TURP, where there was no evidence of cerebral oedema, hyponatraemia or water intoxication. The perception of light and blink reflex was preserved, but the pupillary response to light and accommodation were absent. This suggests that the blindness in all these four cases was due to retinal dysfunction.

Electroretinograms are abnormal in patients with visual impairment who have high serum glycine levels following TURP, independent of reduced serum sodium,[1,2] while visual evoked potentials are not consistently affected.[2] Glycine, just like gamma aminobutyric acid, is a inhibitory neurotransmitter in the retina. (It increases chloride conductance).[3]

When used as an irrigant for TURP, 1.5% glycine, which contains 1000 times the normal concentration of glycine in plasma, has been shown to result in a 100-fold elevation in serum glycine levels without corresponding changes in serum sodium and osmolality, and has been shown to be toxic both to the retina,[4] and the heart.[5]

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Extracorporeal pseudoaneurysm: an unusual complication of radial artery cannulation

During an emergency aortic aneurysm repair, a 77-year-old male had a 20 gauge cannula (Abbocath, Abbott) placed in the right radial artery. Continued bleeding from the skin puncture site postoperatively prompted removal of the cannula. The puncture site was cleaned with isopropyl alcohol and dressed with a knitted viscose dressing impregnated with povidone–iodine ointment 10% (Inadine, Johnson and Johnson) and a nonadherent absorbant dressing (Melonin, Smith and Nephew) held in position with adhesive tape. Four days later the dressing was carefully removed revealing a lesion 4 mm in height and 10 mm in diameter which was pulsatile and expansile in time with the patient's heart rate. (Fig. 1) The radial pulse was palpable distal to the lesion. Following inspection, the lesion was covered with a pressure dressing to prevent accidental rupture and to encourage thrombosis. The patient subsequently died from multiple organ failure some days later. It is assumed that following application of the first dressing, continued bleeding from the arterial puncture site was contained by the viscose dressing. This provided

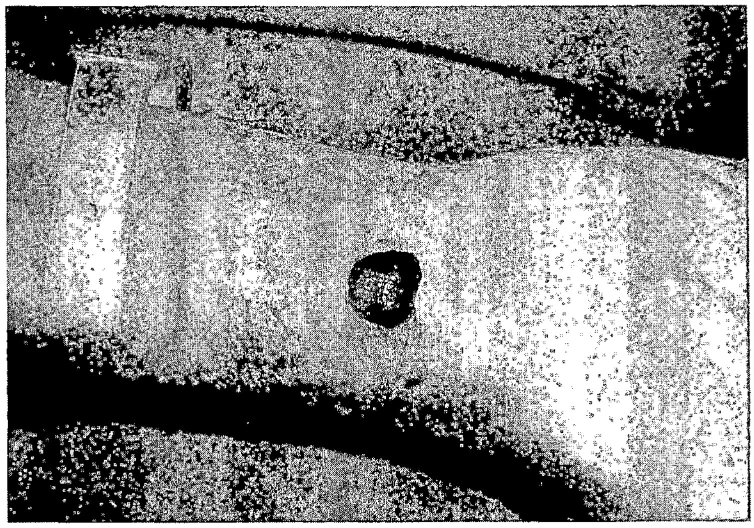

Fig. 1.

the necessary conditions for coagulation and organisation of only the periphery of the extravasated collection of blood, whilst the centre remained in communication with the radial artery thus forming an 'extra-corporeal' pseudoaneurysm.

Both pseudoaneurysm and arteriovenous fistula formation are well recognised complications of radial artery cannulation,[1,2] but there are no reports of extracorporeal pseudoaneurysm formation. I believe that the use of a dressing which did not provide sufficient pressure over the skin puncture site and the presence of sepsis-related coagulopathy were contributory to the formation of the lesion described in this case. It is recommended that arterial puncture site dressings provide sufficient pressure to discourage the continued extravasation of blood following removal of the cannula.

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Bubbles may be deceiving

A postoperative neurosurgical patient required enteral nutrition via a fine-bore nasogastric feeding tube. The 1 mm internal diameter tube was passed easily through the nose and the introducer removed. Correct placement was ascertained by auscultating over the stomach. A 10 ml syringe was used for this and the clinician was satisfied that bubbling could easily be heard. No fluid could be aspirated through the tube but no further test was considered necessary. However, when enteral nutrition was commenced the fluid did not flow easily and the position of the tube was queried. When a 2 ml syringe was used no bubbling could be heard in the stomach, but with a 10 ml syringe one could easily be convinced that the tube was correctly placed. A chest radiograph (Fig. 1) showed the tube to be doubled back on itself, within the oesophagus, with the tip lying well above the stomach.

A simple method of confirming the correct position of a nasogastric tube without resorting to X rays is obviously desirable. One could perhaps be forgiven for thinking that the inability to aspirate stomach contents through a fine-bore tube does not necessarily mean that the tube is not in the stomach. We would like to remind your readers that the syringing of air down the tube is a subtle technique and by using too large a syringe one is very likely to get some air entering the stomach if the tube is in the oesophagus. Indeed the manufacturers recommend a small syringe (2 ml) which highlights a salutary lesson, always read the instructions!

Fig. 1.

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Severe earache following nitrous oxide anaesthesia

A 6-year-old boy was scheduled for an umbilical hernia repair as a day case. He was well pre-operatively, with no recent history of upper respiratory tract infection. Anaesthesia was induced with thiopentone and maintained with oxygen, nitrous oxide and isoflurane with spontaneous respiration via a mask and airway. The wound was infiltrated with bupivacaine. Postoperatively there were no problems, but over the next couple of hours he started to complain of severe unilateral earache, unrelieved by Disprol syrup. The drum on the affected side was not visible due to wax. The child was examined by an ENT surgeon within 3 hours of the anaesthetic, who visualised the drums after removal of the wax and severe inward 'tenting' of both ear drums was observed, but with no sign of perforation. The pain gradually resolved over the next 5–6 hours.

Nitrous oxide has been shown to diffuse into the middle ear during anaesthesia,[1,2] causing pressure changes which have been measured by tympanometry.[3] It has been suggested that this raised pressure can cause barotrauma peroperatively.[4] Sensorineural deafness due to labyrinthine membrane rupture has been described[5] and some authors have suggested that it can alter the nature of the effusion in cases of otitis media, though this is still debated.[3] In most instances it would be presumed that any peroperative pressure change tends to correct itself in the immediate postoperative period. This, however, would seem not to be so in the case described. Presumably in this child the Eustachian tube had acted as a one-way valve, allowing relief of the raised middle ear pressure peroperatively, but not allowing air back in to replace the nitrous oxide as it was resorbed, thus causing indrawing of the ear drums and transient earache.

The child was reviewed 6 weeks postoperatively and there have been no further problems.

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Problems of awareness

The study by Lui and colleagues (*Anaesthesia* 1991; **46:** 435–7), provides a timely reminder that awareness can still occur under anaesthesia. Having presented the case for early recognition and treatment of awareness to the Linkman Conference at Swansea in 1989, I have seen five further patients who have been aware during anaesthesia. Two patients were seen by the anaesthetist concerned within one hour of recovery from the anaesthetic, while two patients told nobody of the awareness before returning home. Four of the patients were given a detailed explanation of the causation of the awareness and were counselled by me, but two patients still needed to be referred to a psychiatrist. All the patients felt that they had benefited from treatment given and that their traumatic stress disorder had been alleviated. Significantly, none of the patients are considering legal action.

A major problem for patients who have suffered awareness is the need for a subsequent anaesthetic. I believe that the facility for these patients to be able to talk to their counsellor, before a subsequent anaesthetic, enables them to cope with the anxiety generated. Indeed for two patients this marked a turning point in their recovery.

While the usual cause of awareness is failure to give an adequate amount of anaesthetic, due to misjudgement or equipment failure, I would like to report another mechanism whereby stress may occur. Suxamethonium has been given to conscious patients on two occasions, once by mistake and once where water was given in mistake for methohexitone. Severe pain and paralysis resulted from these mistakes and a major stress disorder developed in one case. Finally, a syringe of a cephalosporin was mistaken for thiopentone; fortunately the anaesthetist realised that the patient was not anaesthetised and no harm was done.

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Adaptors for microcatheters

I would like to comment on behalf of Kendall on the letter from Dr Eldor and colleagues (*Anaesthesia* 1990; **45:** 1098) regarding Kendall's CoSpan Catheter and the compatible SafeTrak Adapter.

The authors refer to the catheter as being 26 gauge. As a point of clarification, the Kendall CoSpan continuous spinal kits and trays are only supplied with a 28 gauge catheter, as this size and Kendall's design allows for aspiration of cerebrospinal fluid to confirm catheter placement. In responding to the described situation where the authors were not able to reconnect the adapter to the catheter once it became dislodged, it is important to note that to ensure better maintenance of a sterile injection site, the SafeTrak adapter is specifically designed so that it cannot be reconnected should it become detached from the catheter. Kendall does supply sterile adapters, separately packaged, to address this type of situation.

Kendall was concerned to hear that the catheter became dislodged from the adapter during high pressure injection with the 1 ml syringe. Noting that 1550 kPa pressure can be generated by the 1 ml tuberculin syringe, a secure connection will be achieved by tightening down the adapter three full rotations, until the two halves can no longer be rotated. The words 'Safe and Trak' must line up, as shown in the instructions for 'SafeTrak'.

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Paediatric blood pressure and anaesthesia

Dr Mather's case report (*Anaesthesia* 1991, **46:** 381–2) highlights the potential dangers of ignoring or 'explaining away' an unexpectedly high pre-operative blood pressure reading in an apparently healthy child. Unfortunately the subsequent discussion makes no reference whatsoever to another 'clue' available before surgery suggesting that the child in question was not as well as she initially appeared. Her weight (17 kg) was below the third centile for a 7-year-old girl[1] yet would seem to have been ignored. It is incumbent upon each of us to consider all available information before taking a decision to induce anaesthesia; it is probable that the sequence of events described would have been avoided if this had been done in the case of Dr Mather's patient.

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Reference

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A reply

I thank D. J. Warde for his correct comment about considering all the available information before induction. The anaesthetist concerned visited the child pre-operatively; she had appeared well, very active, and her history gave no cause for concern. The child's weight had not been recorded and nursing staff were reminded to do so before her transfer to the operating theatre. In the anaesthetic room the anaesthetist noted she was 17 kg and proceeded to induce anaesthesia; for a 7-year-old girl (by 16 days) this was not considered an unreasonable weight at the time. The anaesthetist is a senior member of staff but only an occasional paediatric anaesthetist. On admission, any young child should have his/her weight accurately checked off a centile chart, which should be readily available on paediatric surgical wards. Paediatricians would routinely have done so and would perhaps have averted the sequence of events that followed.

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Indwelling intramuscular cannula for postoperative analgesia

There has been considerable interest in postoperative analgesia generated by the recent report from the Royal College of Surgeons of England.[1] The most common form of analgesia offered is intermittent bolus intramuscular injections of opioid, usually via a 20 gauge, 40 mm long needle. This has all the disadvantages of multiple injections: fear of pain, trauma to skin and muscle, haematama formation and introduction of infection.

I would like to report the use of an indwelling Teflon FEP cannula placed intramuscularly as a portal for intermittent bolus injections of opioids. A 21 gauge, 25 mm long Wallace Y-Can cannula (H. G. Wallace Ltd, Colchester, Essex) is placed at a safe site in the thigh of the patient and secured with clear plastic dressing. Injections, after test aspiration for blood, are performed by nurses as normal. The cannula is removed when the need for injected opioids is diminished, usually 24–48 hours postoperatively. It has met with enthusiasm by patients and nurses for the painfree injections once the cannula is in place. The advantage of a single puncture wound has also been remarked upon. H. G. Wallace Ltd. have kindly agreed to provide prototypes of a 21G Y-Can cannula of longer length in order to match the usual needle length required to reach muscle in fat thighs.

I do not claim to be the originator of this technique, but a computer assisted literature search (Medline) has not revealed any publications since 1966 on this topic. It is a useful technique to promote adequate uptake of the offer of analgesia after surgery.

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Reference

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Pilo-erection in anaphylactoid reaction

We would like to report a case of pilo-erection occurring as the first manifestation of an anaphylactoid reaction to induction of anaesthesia. A 28-year-old female patient, ASA 1, presented for wisdom teeth extraction. Her only previous general anaesthetic at age 5 years had been uneventful, although details were unavailable. Premedication with oral temazepam 10 mg was given one hour prior to surgery. Anaesthesia was induced with intravenous fentanyl 25 μg, thiopentone 300 mg and followed by suxamethonium 100 mg. Almost immediately intense pilo-erection was noted with 'gooseflesh' appearance of both forearms. This was sufficiently marked to cause one of us to draw the other's attention to it. The patient then rapidly developed a severe anaphylactoid reaction with intense bronchospasm, unrecordable blood pressure and facial oedema. She was successfully resuscitated with intravenous adrenaline (total 500 μg) oxygen, and intravenous fluids (1.7 litres of Haemaccel). Subsequent skin prick testing has revealed a reaction only to suxamethonium.

A literature search found no reports of association of pilo-erection with anaphylactoid or major drug reactions, and our local immunologist (who has investigated the patient) confirmed that he knew of no association between them. Pilo-erection is effected by the contraction of the arrectores pilorum muscles of the hair follicles, and has been classified as an alpha-one adrenoceptor action. It has been described in phaeochromocytoma,[1] and in association with the administration of various drugs including methoxamine, midodrine, tolazoline, nicotinic acid, and

labetolol,[2] as well as in response to cold, acute fear and narcotic abstinence syndrome. None of these was applicable in this case. It has also been described in response to mast cell degranulation in rats.[3]

We would be interested to know if any readers have noticed pilo-erection in association with drug reactions. Might pilo-erection be a useful warning of a potentially life-treating situation?

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Blood pressure cuff changeover in paediatric anaesthesia

During routine paediatric anaesthesia noninvasive blood pressure measurements are required on a wide age range of patients. Critikon have a selection of Disposa-cufs (sizes 1–5) for use in neonates. These are attached to the pneumatic hose by pressing the connectors into a connector 'head' (Fig. 1). For infants and children a range of Duracufs are available which require a different pneumatic hose, which has screw-on connections (Fig. 1). During the rapid patient turnover of a busy operating list, frequent changing of the pneumatic hoses at the back of the Dinamap vital signs monitor is time consuming and produces significant wear and tear on the connections. Using silicone tubing, two 3-way taps, two female connectors taken from old perished pneumatic hose and four male connectors from old blood pressure cuffs, we have made a simple tap system which allows for easy and efficient changeover between pneumatic circuits (Fig. 2).

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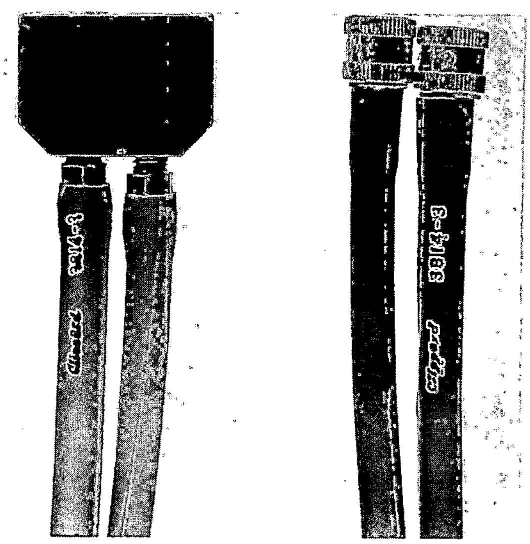

Fig. 1. Press-in connector 'head' for neonatal cuffs on left. Screw-on connector for all other cuffs on right.

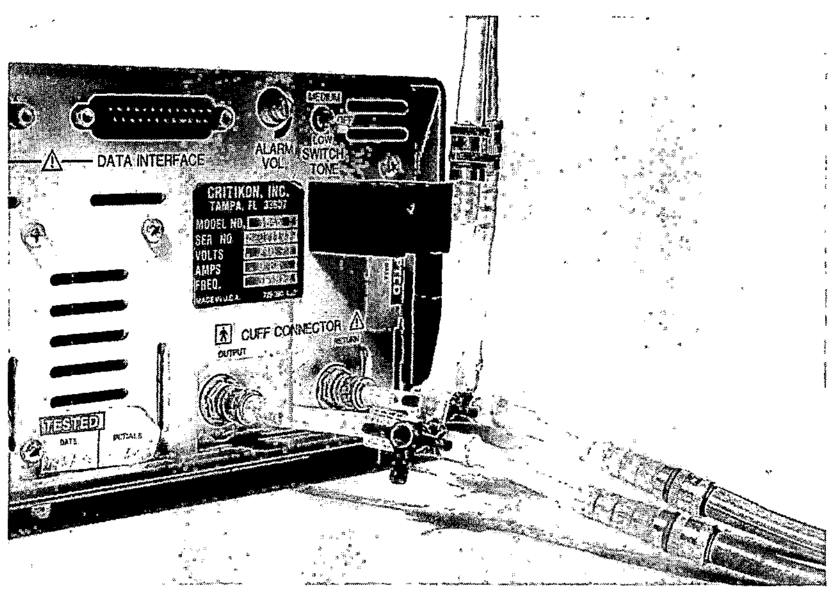

Fig. 2. Simultaneous attachment of both pneumatic circuits with 3-way tap allowing for selection of circuit being utilized.

Acoustic monitoring of arterial blood pressure

In a recently published letter, Dr Gilston mentioned two major facilities that he would like to see added to monitoring equipment (*Anaesthesia* 1991; **46:** 420). In the first place he would like to have an acoustic signal that differentiates between the heart rate derived from the ECG, and the peripheral pulse rate (obtained by means of pulse oximetry). In the second place, he underscores the importance, during invasive arterial blood pressure

monitoring, of having an audible signal representing the systolic pressure.

We reported, unfortunately only in German, on such a latter facility a number of years ago in a short contribution to a congress.[1] In it we described how we provided conventional pressure amplifiers with a supplementary device (Pressure Sound Converter 782, Schabert Instrumente SIR, D-8551 Röttenbach, Germany) which, at each pressure pulse is capable of converting, selectively, the following pressure values into audible signals: systolic diastolic or mean pressure, systolic *and* diastolic pressure, and the entire course of the pressure pulse (continuous signal). In addition, a reference signal of 1000 Hz can be generated, which corresponds to a pressure signal of 100 mmHg. This device has been employed clinically in the fields of cardiac, vascular and neurosurgery. It was established that the audible signal permitted sensitive and rapid monitoring of the arterial pressure without the need to watch the monitor continuously. The simultaneous signalling of systolic *and* diastolic pressure by means of two short sounds, and the continuous acoustic signalling of the entire pressure curve both have a disquieting effect; an audible signal for the diastolic pressure is of no clinical importance here. This means that the selection can be limited to systolic and mean pressures. The capability for acoustic monitoring of the arterial pressure by a short audible signal of pressure-proportional frequency considerably expands the on-line monitoring possibilities in critical situations, and the need to turn one's eyes away from other urgent tasks is obviated.

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Reference

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Capnography and the Bain coaxial breathing system

Capnography is now well established as an essential monitor during general anaesthesia. However, it is not always employed in clinical practice owing to insufficient funding or simple disregard of the Association's recommendations, frequently because the operation is expected to be short and straightforward. Hence, I wish to draw attention to a particular clinical application of capnography which involves the early detection of disconnection at the proximal end of the inner tube of the Bain co-axial breathing system.

A 22-year-old, 55 kg woman (ASA 1) underwent a routine excision of a small neck lump. Anaesthesia was induced with propofol 150 mg and fentanyl 0.1 mg. A laryngeal mask was inserted and she was allowed to breathe spontaneously through the Bain system, using isoflurane in nitrous oxide and oxygen. Monitoring included a pulse oximeter, noninvasive blood pressure, ECG, inspired oxygen concentration and capnography. Following the surgical incision, the patient was noted to hyperventilate markedly and the capnograph alarmed indicating gross rebreathing with an end-tidal CO_2 of 8.3 kPa. All other measurements were normal. It was initially thought that the hyperventilation might have been due to a combination of light anaesthesia and an inadequate fresh gas flow. The latter was increased from 9 to 18 litres/minute and the isoflurane concentration from 2 to 4%. These manoeuvres did not result in any response after approximately 5 minutes. Meanwhile, the following checks were carried out. The CO_2 Rotameter and cylinder were in the 'off' position. To ensure that there was no leakage the CO_2 cylinder was removed from the anaesthetic machine. The breathing system had appeared intact. However, only a close-up inspection managed to reveal a proximal disconnection of the inner tube, which had remained in contact with the metal gas outlet. The increased equipment deadspace had resulted in failure of CO_2 elimination. The disconnection was rectified and the anaesthesia proceeded uneventfully.

This particular incidence of disconnection occurred inadvertently in the middle of an operating list, despite a standard check of the breathing system before the commencement of the list and a visual check before connecting the breathing system to the patient. Capnography enables the monitoring of sudden changes, such as disconnection, leaks and obstruction in the breathing system. The diagnosis of the above disconnection hazard might otherwise have been less rapidly detected without the monitoring in use on this occasion. Inappropriate management and the potential deleterious consequences of hypercapnia were thus avoided. The above critical incidence emphasises the importance of the standards of minimum monitoring.

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Caudal buprenorphine in children: where should they be nursed?

Epidurally injected opioids are known to provide excellent and long lasting analgesia postoperatively. In a recent study, Girotra and colleagues (*Anaesthesia* 1990; 45: 406–8) compared the quality and duration of analgesia after caudal blocks performed with either bupivacaine 0.25% (1.25 mg/kg) or buprenorphine (4 μg/kg) in children who had undergone genito-urinary surgery. Buprenorphine proved to be more effective than bupivacaine in the late postoperative phase, the analgesia lasting from 20 to more than 24 hours, with fewer side effects.

In 1988, Ready *et al.*[1] reported their experiences with a postoperative pain management service, where opioids were administered epidurally on ordinary wards. Commenting on this article, Bromage[2] warned against use of epidural opioids on ordinary wards where continuous respiratory monitoring is not guaranteed. Although it rarely occurs, respiratory depression is nevertheless a potential danger associated with opioid injection near the spinal cord.

Other authors have also called attention to this danger and have demanded suitable respiratory monitoring.[3–7] We fully agree with this warning and recommend that, especially in children, epidural opioids should only be administered if the patient is transferred postoperatively to an intensive care unit or a suitable recovery ward.

In the study reported by Girotra *et al.*, 21 of the 40

children underwent circumcision. After such operations, the children are generally transferred to an ordinary ward where there is usually no guarantee of adequate respiratory monitoring. We are therefore of the opinion that the procedure described by these authors should not be routinely used and under these conditions we plead for caudal blocks to be performed with a local anesthetic.

For operations on the penis, the question also arises, whether it would not be preferable to use procedures with fewer side effects than a caudal block, as, for example, the penile nerve block[8,10] or the topical application of 10% lidocaine spray.[7]

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Peri-operative management of diabetes mellitus

The continuous glucose–insulin–potassium (GIK) infusion regimen (Table 1) is a standard and a widely adopted technique in the peri-operative management of patients with diabetes mellitus.[1] It is stated that the standard Alberti's GIK regimen has the disadvantage of having a fixed insulin concentration, so that the entire bag must be changed each time the plasma glucose is outside of targeted values.[2,3] We would like to describe a simple technique which can overcome the above mentioned problem.

In two separate 10 ml syringes, plain insulin and potassium chloride (KCl), are prepared in the concentration of 1 unit/ml and 1 mmol/ml respectively. A 100 ml measured volume set is attached to either a 500 ml or 1 litre 10% glucose bag and 100 ml is transfered into the set. This set has also a port for adding drugs. Two mmol of KCl is added to this 100 ml of 10% glucose while the amount of insulin added is altered according to the blood glucose value (measured every one hour by a Dextrometer) as given in the table. This GIK mixture in the measured volume set is connected to an infusion pump and adjusted to deliver 100 ml/hour. Alternatively 2.4, 2.8, 3.2, 3.6 and 4 units of plain insulin may be added to 100 ml of 10% glucose for blood glucose values (mmol/litre) of < 4.4, < 6.7, 6.7–10, > 10 and > 15 respectively if one follows the 10% glucose protocol of Alberti's regimen.[4]

Our experience with this regimen is over 30 diabetic patients undergoing major noncardiac surgical procedures performed under general anaesthesia has yielded satisfactory results (unpublished). The ratio of insulin per gram of glucose in this protocol remains in the acceptable range of 0.2 to 0.4. This modified protocol is simple to use, cost effective and overcomes the problem encountered in the standard Alberti's GIK regimen.

Table 1. Glucose – insulin – potassium (GIK) protocol.

Blood glucose mmol/litre	Fluid 100 ml/hour	Insulin U/100 ml	KCl mmol/100 ml
5–10	10% glucose	2	2
10–15	10% glucose	3	2
> 15	10% glucose	4	2

Nizanis Institute of Medical Sciences, Hyderabad 500482 India

S. MANTHA
S.M. RAO

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First anaesthetics in the world

In my article "forty-six 'first anaesthetics' in the world",[1] I have inadvertently included some wrong information concerning Glasgow and Edinburgh. In the Proceedings from the History of Anaesthesia Society 1989,[2] A. G. Macdonald pointed out that Dr John Henry Hill Lewellin (1818–86) gave the first ether anaesthetic in Glasgow to a 23-year-old man for a molar extraction on 4 January 1847, in his private practice. The anaesthetic I have mentioned as the first in Glasgow took place on 10 January and was the first ether anaesthesia in the Royal Infirmary when Dr

Laurie (?) removed a tumour from the elbow.

I was also wrong about the first anaesthetic given in Edinburgh. Through help from Dr Richard H. Ellis, London, and Dr Alstair H. B. Masson, Edinburgh, I now know that the first anaesthetic with ether took place in The Royal Infirmary on 9 January, 1847 when Dr James Duncan (1812–66) amputated the leg of a young man. The anaesthetic I mentioned was the second in Edinburgh and took place in the same hospital on 17 January when Professor James Miller (1812–64) operated on a sustained, compound fracture of the tibia in a 43-year-old Irish labourer. Further information can be obtained from Barry C. Howell and James Wilson,[3] Richard H. Ellis[4] and A. G. Macdonald in the above mentioned article.

It can therefore be stated that ether was used for anaesthesia 6 days earlier in Glasgow than in Edinburgh.

Let me add two more 'first anaesthetics' which have appeared after publication of my article. Professor B. T. Finucane, Edmund, Canada has informed me about the first use of ether in Dublin[5] when Dr John MacDonnell (?) amputated the arm of an 18-year-old girl on 1 January in Richmond Hospital.

The other was sent me from Dr Aurel Mogoseanu, Timişoara, a now well known town in Romania. On 5 February 1847 Dr Musil (?) and chief surgeon Siess (?) amputated a finger on an enlisted soldier, Nikola Muntyan, in the Military Hospital. The patient inhaled ether from an apparatus designed after the illustration in *London Illustrated Gazette (News)* of 9 January 1847. At that time Timişoara was the capital of the Banat province in the Austria-Hungary Empire.[6] May I also correct two further points. Dr A. Franco Grande, Santiago, has been so kind as to tell me that the first ether anaesthetic in Spain was given on 13 February and not 14 in 1847, in the surgical clinic of the University Hospital, Madrid when Professor Diego de Argumosa (1792–1865) operated on a large parotid abscess.[7] I have also written that Professor A. J. Jorbet de Lamball Paris (1799-) died in 1847 when it should be 1867, and Professor Demme's first names are Herman Askan.

Overlaege Ved Rigshospitalet,
Kirkehoj 4-2900
Hellerup

O. SECHER

References

1. SECHER O. Forty-six 'first anaesthetics' in the world. *Acta Anaesthesiologica Scandinavica* 1990; **34:** 552–6.
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Anaesthesia, 1991, Volume 46, pages 902–903

Obituaries

Donnelly, P.B., MB, BCh, FFARCS, FFARCSI, formerly Consultant Anaesthetist, Daisy Hill Hospital, Newry, County Down. Qualified from Queen's University Belfast, 1959.

Butterworth, H.C., MB, BS, FFARCS, formerly Consultant Anaesthetist, Darlington district group of hospitals. Qualified from Durham University, 1946.

Elliott, G.W., MB, BS, FFARCS, formerly Consultant Anaesthetist, Ashington Hospital, Northumberland. Qualified from Durham University, 1954.

International congress calendar

1991

2–4 October. Rotterdam, The Netherlands. *12th International Symposium on Computer Assisted Decision Support and Database Management in Anesthesia, Intensive Care and Cardiopulmonary Medicine.*
Information: Dr Omar Prakash, Thoracic Centre, Dijkzigt Hospital, Dr Molewaterplein 50, 3015 GD Rotterdam, The Netherlands.

26–30 October. San Francisco. *American Society of Anesthesiologists Annual Meeting.*
Information: Executive Secretary, ASA, 515 Busse Highway, Park Ridge, IL 60068, USA.

3–9 November. Poipu Beach, Kauai, Hawaii. *California Society of Anesthesiologists Hawaiian Seminar.*
Information: California Society of Anesthesiologists Educational Programs Division, 1065, East Hillside Boulevard, Suite 410, Foster City, California 94404-1615, USA.

6–9 November. Kuala Lumpur. *7th Asian Congress of Anaesthesiologists.*
Information: Dr S.W. Lim, Pantai Medical Centre, 59199 Kuala Lumpur, Malaysia.

8–10 November. Vina del Mar. *2nd Congress of Fed. of South American Socs. of Anesthesiologists.*
Information: Dr Guillermo Lema, Av. Providencia 1476 (Depto. 405) Santiago, Chile.

8–11 November. Toronto. *Paediatric Anaesthesia Conference.*
Information: Sheila M. Peart, Paediatric Anaesthesia Conference, The Hospital for Sick Children, 555 University Avenue, Toronto, Ont M5G 1X8.

19–22 November. Rotterdam, The Netherlands. *7th International Symposium on Cardiopulmonary Urgencies and Emergencies.*
Information: Dr O. Prakash, Thorax Centre, Dijkzigt Hospital, Dr Molewaterplein 50, 3015 DG, Rotterdam, The Netherlands.

26–28 November. Doha-Qatar. *First Gulf Conference on Intensive Care Medicine.*
Information: Dr Jamal S. Al-Shanableh, Hamad Medical Corporation, P.O. Box 3050, Doha, State of Qatar.

1–4 December. Bangkok. *6th Congress of Western Pacific Association of Critical Care Medicine.*
Information: Dr P. Sakolsatayadorn, Surgery, Siriraj Hospital, Bangkok 10700, Thailand.

6–8 December. Washington. *Washington State Society of Anesthesiologists Annual Meeting.*
Information: Washington State Society of Anesthesiologists, 2033 Sixth Avenue, 804, Seattle, Washington 98121, USA.

7–11 December. New York. *Forty-fifth Postgraduate Assembly in Anesthesiology.*
Information: Kurt G. Becker, Executive Director, The New York State Society of Anesthesiologists Inc., 41 East 42nd Street, Suite 1605, New York 10017, USA.

1992

19–21 January. Honolulu, Hawaii. *Second American-Japan Anesthesia Congress.*
Information: Vicky Larsen, Department of Anesthesiology, University of Utah School of Medicine, 50 North Medical Drive, Salt Lake City, UT 84132, USA.

22–26 January. Acapulco, Mexico. *4th International Symposium, Anesthesia for Cardiac Patients.*
Information: Helen Phillips, Mount Sinai Medical Center, 1, Gustave L, Levy Place, Box 1010, New York, NY 10029-66574, USA.

1–8 February. Colorado. *18th Annual Vail Conference in Anaesthesiology.*
Information: Sonya Craythorne, Professional Seminars, P.O. Box 012318, Miami, Florida 33101, USA.

1–8 February. Steamboat Springs, Colorado, USA. *New Horizons in Anesthesiology.*
Information: Ms Kathleen A. Maitland, Department of Anesthesiology, Emory University at Crawford Long Hospital, 25, Prescott Street, 5405, Glenn Atlanta, GA 30308, USA.

8–14 February. Cooper Mountain, Colorado, USA. *Anesthesia Update 1992.*
Information: Alan H. Goldberg, Department of Anesthesiology, Medical College of Wisconsin, 8700W Wisconsin Avenue, Milwaukee, Wisconsin 53226, USA.

3–6 March. Boston Massachusetts. *14th Annual Meeting, Society of Cardiovascular Anesthesiologists.*
Information: SCA, P.O. Box 11086, Richmond, VA, 23230-1086, USA.

13–17 March. San Francisco. *66th Congress of the International Anesthesia Research Society.*
Information: Anne F. Maggiore, International Anesthesia Research Society, 2 Summit Park Drive, Suite 40, Cleveland, Ohio 44131, USA.

25–29 March. Tampa. *17th Annual Meeting of the American Society of Regional Anesthesia.*
Information: ASRA, P.O. Box 11086, Richmond, Virginia, 23230-1086, USA.

29 March–2 April. Atlanta, Georgia. *The Third International Symposium on the History of Anaesthesia.*
Information: R.K. Calverley, Medical Center, University of California, 225 Dickinson Street, San Diego, California CA 92103, USA.

1–3 April. Bristol. *Junior Anaesthetists' Group Linkman Conference and Annual Scientific Meeting.*
Information: The Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London WCIB 3RA, UK.

23–25 April. Atlanta, Georgia, USA. *2nd International Symposium on Memory and Awareness in Anesthesia.*

Information: Mrs Kathleen A. Maitland, Department of Anesthesiology, Emory University at Crawford Long Hospital, 25 Prescott Street, 5405 Glenn, Atlanta, GA 30308, USA.

2–6 May. Boston. *Society of Cardiovascular Anesthetists.*
Information: P.O. Box 11086, Richmond, Virginia 23230-1086, USA.

21–24 May. Montreal, Canada. *4th International Neuromuscular Meeting.*
Information: Clair Diano, Post-Graduate Board, Royal Victoria Hospital, 687 ouest, Avenue des Pins, Montreal, Quebec H3A 1AI, Canada.

5–9 June. Toronto. *49th Annual Meeting of the Canadian Anaesthetists' Society.*
Information: Ms Kara Kieferle, Meeting Coordinator. 1 187 Gerrard Street E, Toronto, Canada M5A 2E5.

9–12 June. Brussels, Belgium. *4th Joint Meeting, European and American Societies of Regional Anesthesia.*
Information: ESRA, Dr van Zundert, Kempenlaan 12, B-2300 Turnhout, Belgium or ASRA, P.O. Box 11086, Richmond VA 23230-1086, USA.

7–12 June. Barcelona. *Anestesia 92.* *Information:* Pacifico, S.A.: c/Muntaner, 112 08036-Barcelona, Spain.

10–13 June. Brussels. *European Society of Regional Anaesthesia (UK) Meeting.*
Information: The Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London WC1B 3RA, UK.

10–12 June. Rotterdam, The Netherlands. *13th International Symposium on Computer Assisted Decision Support and Database Management in Anesthesia, Intensive Care and Cardiopulmonary Medicine.*
Information: Dr Omar Prakash, Thorax Centre, Erasmus University, 3000 DR Rotterdam, The Netherlands.

11–14 June. Marco Island, Florida. *Annual Meeting of the Florida Society of Anesthesiologists.*
Information: Florida Society of Anesthesiologists, 6501 25 Ways S, Ste D, St Petersburg, FL 33712, USA.

12–19 June. The Hague. *10th World Congress of Anaesthesiology.*
Information: Dr Harm Lip, Nilantsweg, 99, 8041 AR Zwolle, Netherlands.

26–30 August. Poznan, Poland. *European Academy of Anaesthesiology.* (Open) Refresher Course and (Members only) Scientific Meeting.
Information: Professor M.D. Vickers, Department of Anaesthesia, University of Wales College of Medicine, Heath Park, Cardiff CF4 4XN.

9–11 September. Bournemouth. *Linkman and Annual Scientific Meeting.*
Information: The Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London WC1B 3RA.

17–21 October. New Orleans. *American Society of Anesthesiologists Annual Meeting.*
Information: Executive Secretary, ASA, 515 Busse Highway, Park Ridge IL 60068, USA.

20–21 November. Brighton, England. *1st CPR Congress of the European Resuscitation Council.*
Information: Dr D.A. Zideman, Department of Anaesthesia and Critical Care, Hammersmith Hospital, DuCane Road, London W12 0HS, UK.

12–16 December. New York. *46th Postgraduate Assembly in Anesthesiology.*
Information: Kurt G. Becker, Executive Director, The New York State Society of Anesthesiologists, Inc., 41 East 42nd Street, Suite 1605, New York 10017, USA.

1993

30 January–6 February. Aspen, Colorado. *New Horizons in Anesthesiology.*
Information: Miss Kathleen A. Maitland, Department of Anesthesiology, Emory University at Crawford Long Hospital, 25 Prescott Street, 5404 Glenn, Atlanta, GA 30308, USA.

12–16 February. Utah. *38th Annual Postgraduate Course in Anethesiology–'Anaesthesiology: Today and Tomorrow'.*
Information: Vicky Larson, Department of Anesthesiology. University of Utah School of Medicine, 50 North Medical Drive, Salt Lake, Utah 84132, USA.

19–23 March. San Diego, California. *67th Congress of the International Anesthesia Research Society.*
Information: Anne F. Maggiore, Executive Director, International Anesthesia Research Society, 2 Summit Park Drive, Suite 140, Cleveland, Ohio 44131, USA.

29 April–2 March. North Carolina. *Meeting of the Association of University Anesthetists.*
Information: Francis M. James III, Department of Anesthesia, Wake Forest University Medical Center, 300 S. Hawthorne Road, Winston-Salem, North Carolina 27103, USA.

10–13 June. Boca Raton, Florida. *Annual Meeting of the Florida Society of Anesthesiologists.*
Information: Florida Society of Anesthesiologists, 6501 25 Way S. Ste D, St Petersberg, FL 33712, USA.

1–4 September. Liverpool. *European Course and Congress in Paediatric Anaesthesia.*
Information: Dr P.D. Booker, Alder Hey Hospital, Liverpool L12 2AP.

22–24 September. Glasgow. *Linkman Conference and Annual Scientific Meeting. Joint Meeting between the Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London, WC1B 3RA.*
Information: The Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London WC1B 3RA.

9–13 October. Washington DC. *American Society of Anesthesiologists Annual Meeting.*
Information: Executive Secretary, ASA 515 Busse Highway, Park Ridge, IL 60068, USA.

1994

7–9 September. Brighton. *Linkman Conference and Annual Scientific Meeting.*
Information: The Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London WC1B 3RA.

2–7 October. Jerusalem. *European Congress of Anaesthesiology.*
Information: The Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 9 Bedford Square, London WC1B 3RA, UK.

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Safety Action Bulletins

Physio Control Lifepack and Difibrillator/Monitors: Field Retrofit Software Up-Grade (SAB(91)28)

A malfunction has been reported where a flat trace, resembling asystole, was displayed following defibrillation. This can only occur when monitoring through the 3-lead cable immediately after a defibrillation discharge. The patient should be monitored through the paddles until the equipment's software has been updated by the company. Physio Control Ltd have notified all UK customers. There are 284 units in the UK.

Gemini IV solution administration sets codes 2212 and 2243 for use with Gemini series volumetric pumps: disconnection of tubing (SAB(91)29).

Incidents have occurred where the tubing of the IMED Gemini IV solution administration sets (codes 2212 and 2243, manufactured before September 1990) has become disconnected from the drip chamber during use. These sets are dedicated for use with the Gemini series volumetric pumps. Sets with strengthened joins are currently in distribution.

Gardner Medical (GME) medical gas terminal units: risk of malfunction (SAB(91)36)

There have been reports of medical gas terminal units manufactured by Gardner Medical becoming jammed and affecting insertion/retention of the gas probe. This is due to the formation of burrs in the slots which retain the probe retention pins; this restricts pin movement. The units which are no longer in production are identified by their chrome outer rings and in some instances the initials GME are printed on the front gas-identification label.

Hewlett Packard 78352 and 78354 Series ECG/PB monitors: modification (SAB(91)43)

These patient monitors with the non-invasive blood pressure (NIBP) option, may malfunction due to an intermittent fault. Malfunction is indicated by the NIBP pump intermittently stopping with partial inflation of the cuff, error code E47 or E17 appearing; ECG waveform disappearing when NIBP pumps and error code E10 or E20 appearing. This lasts for a few seconds, while a 'warm start' is initiated and results in resetting the monitor with correct patient data. The manufacturers will fit a filter board, free of charge, which removes electrical interference produced by the pump, and will do this on any unit even though no symptoms may have been experienced. All models supplied since June 1990 have had the filter board fitted during manufacture.

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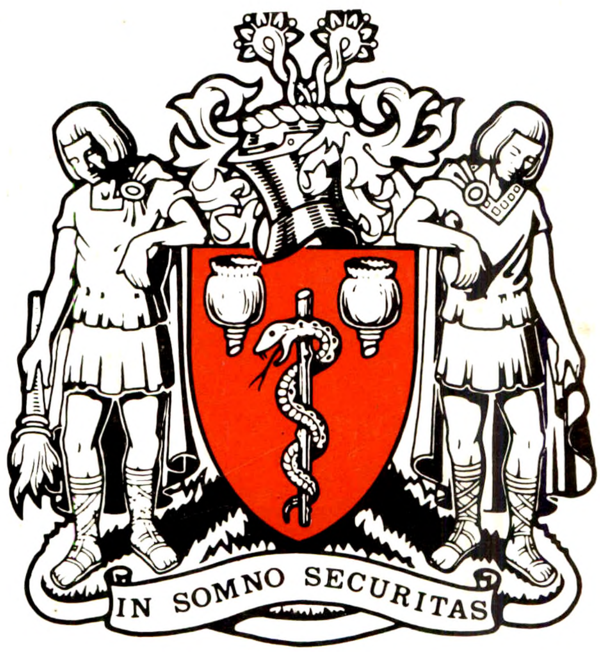

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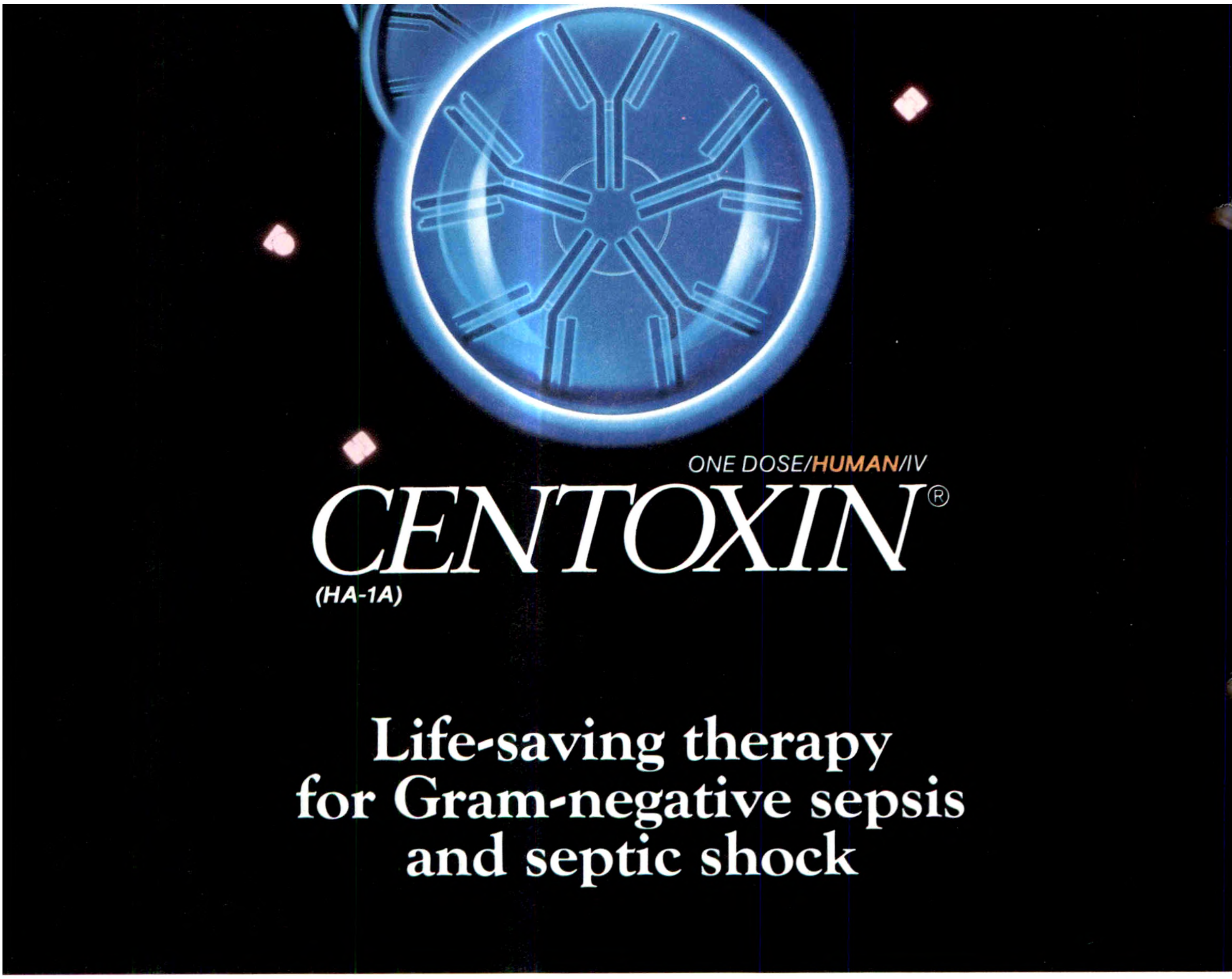

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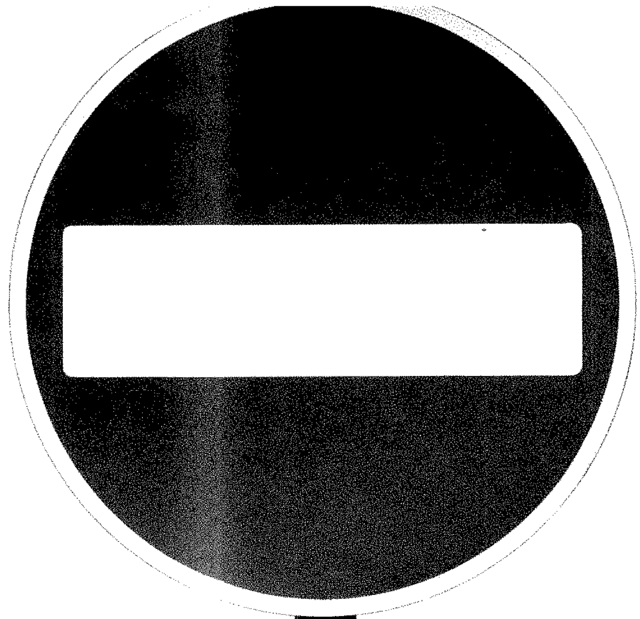

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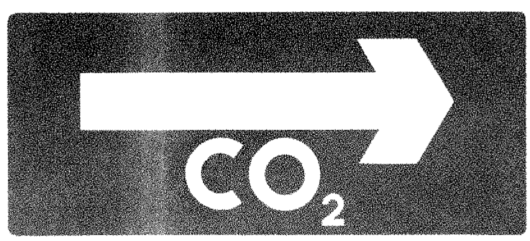

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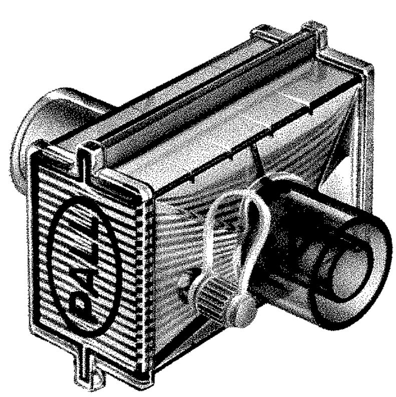

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Anaesthesia, 1991, Volume 46, pages 905–906

Editorial

Supplementary oxygen—potential for disaster

The administration of supplementary oxygen is a commonly employed therapeutic measure which should be of benefit to the patient for whom it is indicated. Over recent years, however, the Safety Committee of the Association of Anaesthetists has noted with growing concern a number of related incidents in which disastrous accidents, often fatal, have occurred as a result of the way in which the oxygen was administered. This editorial is designed to bring to the anaesthetist's attention some of the ways in which these problems have arisen. It is hoped that by being made aware of the potential dangers, measures can be taken to avoid them, and that this training can then be extended to those for whose practice we are responsible.

The administration of supplementary oxygen is indicated in a variety of situations where the patient is either already hypoxic or potentially at risk of becoming so. There are several accepted ways in which oxygen may be administered. The commonest means is a clear plastic facemask applied over the patient's nose and mouth. Simple oxygen facemasks have a variable performance, but when supplied with a flow of oxygen of 4–5 litres/minute provide a simple and effective way of raising the inspired oxygen concentration to approximately 40%. Oxygen facemasks of this nature are routinely used, not only by anaesthetists and other doctors, but also by nurses, paramedics and ambulance personnel. The only contraindications to using such a simple device arise when the percentage of oxygen required is greater than the mask can deliver, when the patient is in chronic respiratory failure and is dependent on a hypoxic drive or when the patient is in acute respiratory failure and needs assisted ventilation.

However, sometimes other simple means of supplying additional oxygen are employed. These include nasal cannulae which are inserted into the nares, and the use of a nasal catheter which is inserted further back into the nose towards the nasopharynx.

It is difficult at first to imagine how these simple devices could prove dangerous. The oxygen normally available from an outlet on the wall is supplied by the hospital piped oxygen delivery system at a nominal pressure of 400 kPa. This pressure of four atmospheres or four bar is not normally considered in relationship to airway pressure, but it is a salutary exercise to convert 400 kPa into centimetres of water pressure and to realize that the oxygen outlet at the wall is supplied at a pressure of over 4000 cm H_2O, or over 200 times the pressure normally used to artificially inflate the lungs! Therein lies the danger. If the flow of oxygen delivered at this pressure is directly coupled to the patient either by accident or design, the consequences may be disastrous.

The mechanism of barotrauma is well known.[1] Alveolar rupture, with pulmonary interstitial emphysema leading to mediastinal emphysema is the normal sequence followed as the high pressure gas disperses. From the mediastinum the gas escapes further afield producing subcutaneous emphysema, bilateral tension pneumothoraces and possibly pneumoperitoneum. Air embolism may ensue and ultimately cardiac arrest will occur. The magnitude of the disaster is related to the rate at which the gas is being supplied as well as the presssure which is generated and the time that elapses before the problem is detected.

How can the administration of oxygen via a facemask cause such a build-up of pressure? It is obvious that the simple application of a facemask is not likely to cause such a train of events. The oxygen must be delivered directly to the lower airway, and there must be some form of restriction to the free outflow of the surplus gas.

Two unusual accidents have come to the Safety Committee's attention. Both concerned patients who had returned from the operating theatre with tracheal tubes in place. On both occasions it was found that by chance the inlet port of the oxygen mask which had been loosely applied over the open end of the tracheal tube had impacted onto the 15 mm male connector of the tracheal tube causing the flow of oxygen of some 5 litres/minute to be delivered directly to the trachea. The danger is of course compounded should the cuff of the tube still be inflated. In the two cases reported to the Safety Committee, one proved fatal and the second patient recovered after sustaining severe barotrauma. A third accident of a similar nature was only avoided by prompt corrective action.

In a fourth case, ambulance personnel had experienced difficulty in keeping the facemask in place over the end of the tracheal tube on a restless patient whose trachea had been intubated and was in transit to hospital. The ambulance staff had resorted to connecting the oxygen supply directly to the cuffed tracheal tube. This patient also died.

The question arises as to why some form of T-piece attachment is not used to supply oxygen safely in these situations? Such attachments are simple to use, inexpensive and would have overcome all the problems described above. The same message must also apply to patients with a tracheostomy tube *in situ*. In any patient returning from the operating theatre with a cuffed tracheal tube in place, it is worth considering whether there are any grounds for maintaining the cuff inflated. If there are none, it would be wise as a routine to deflate the cuff before handing the patient over to the recovery staff.

As an alternative to the use of a facemask, it has been pointed out that nasal cannulae may be employed. These are ideal for long-term use in the conscious patient to raise the inspired oxygen concentration. However, some anaesthetists resort to the use of a longer catheter which may extend well into the nasopharynx in order to administer supplementary oxygen. This may be done in an attempt to use the nasopharynx as a reservoir for the delivered oxygen, thereby raising

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the inspired concentration. The use of a suction catheter or similar device in this manner, however, can be potentially dangerous. The exact position of the tube may often be uncertain. If such a tube descends through the vocal cords, the outflow of gas may become obstructed at any time, and without warning produce disastrous consequences. Furthermore the end of the catheter may migrate elsewhere if inadequately secured. A suction tube, initially placed in the nasopharynx via a nasopharyngeal airway, delivering oxygen at a flow of 4–8 litres/minute, found its way into the oesophagus and the patient died of a ruptured stomach. This is a well known complication of administering nasal oxygen by means of a catheter.[2] It must be emphasised that suction catheters are not designed for the administration of oxygen, and their use for this purpose renders the operator fully responsible for any adverse sequelae that might occur.

The message must be clear. Oxygen is a therapeutic agent with benefits and complications like any other treatment. Its correct use must be fully understood and safe techniques adhered to by anyone who uses it or prescribes its use by others.

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Dose-response relationship and time course of action of Org 9426

A new muscle relaxant of intermediate duration evaluated under various anaesthetic techniques

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Summary

The dose-response relationship of Org 9426, its time course of action and the reversibility of the residual block by neostigmine have been investigated in 100 patients undergoing various anaesthetic techniques. The dose-response was measured immediately following induction of anaesthesia. Doses of Org 9426, required for 50% and 90% depression of the twitch height, were 202 and 328 μg.kg^{-1}, respectively. The clinical duration of the maintenance doses, 150 μg.kg^{-1}, ranged from 9.5 to 13.4 min and from 12.8 to 18.9 min for the first and fifth maintenance doses, respectively. Spontaneous recovery indices (25%–75%) were between 9.5 and 16.7 min; neostigmine methylsulphate administered at 25% recovery of the twitch height promptly reversed the residual block. No side effects were observed. The extent of the influence of the anaesthetic on the time course of Org 9426 appears to be fractional considering the variation of the time course within the separate groups.

Key words

Anaesthetics, gases; nitrous oxide.
Anaesthetics, intravenous; fentanyl, droperidol, propofol.
Anaesthetics, volatile; halothane, isoflurane, enflurane.
Neuromuscular relaxants; Org 9426.

Org 9426 is a new nondepolarising neuromuscular blocking agent with a chemical structure related to that of vecuronium, as shown in Figure 1.

From recent clinical studies Org 9426 appeared to be five to seven times less potent than vecuronium and showed a faster rate of onset of neuromuscular block [1, 2], whereas duration of action and recovery index were found to be similar [2]. Good to excellent intubation conditions were shown within 60 s after approximately 1.5 times the ED_{90} dose [2]. Org 9426, available in a 'ready for use' pharmaceutical presentation, when administered in the clinical dose range, demonstrated no relevant cardiovascular or other side effects either in man [1–3] or animals [4, 5]. This study was designed to evaluate the potency, time course of action, reversibility, cumulative tendency and cardiovascular effects of Org 9426 in patients anaesthetised with five different techniques: nitrous oxide (65%) in oxygen with halothane, enflurane, isoflurane, droperidol/fentanyl or propofol/fentanyl.

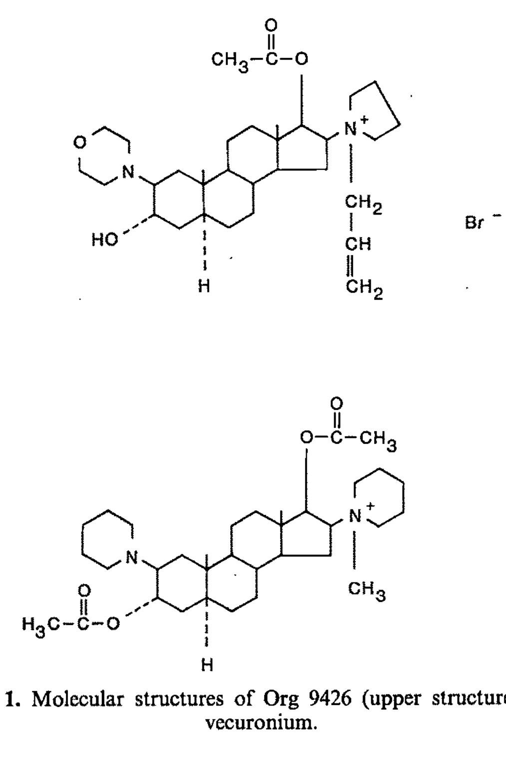

Fig. 1. Molecular structures of Org 9426 (upper structure) and vecuronium.

Methods

Patients

One hundred ASA class 1 or 2 patients, scheduled for elective surgery, aged 18 to 60 years, who gave written

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informed consent, participated in the study, which was approved by the Medical Ethics Committee of the University of Groningen. Patients with known kidney, liver or neuromuscular disorders, or those taking any medication known to interfere with the action of neuromuscular blocking agents were excluded. Five groups of 20 patients each were formed according to the different types of anaesthesia employed.

Anaesthesia

All patients were premedicated with oral midazolam 7.5 mg, approximately 60 min before the expected induction of anaesthesia. In the first three groups of patients anaesthesia was induced with intravenous thiopentone 3–5 $mg.kg^{-1}$ and maintained with 65% nitrous oxide in oxygen and halothane, enflurane, or isoflurane, in end-tidal concentrations according to the need of the patient. In the fourth group anaesthesia was induced intravenously with droperidol 0.1–0.2 $mg.kg^{-1}$, fentanyl 3–6 $\mu g.kg^{-1}$, followed by a small dose of thiopentone 1–2 $mg.kg^{-1}$ and maintained with 65% nitrous oxide in oxygen and incremental doses of fentanyl. In the fifth group anaesthesia was induced intravenously with fentanyl 2–4 $\mu g.kg^{-1}$, and propofol 2–2.5 $mg.kg^{-1}$, and maintained with 65% nitrous oxide in oxygen, a continuous infusion of propofol 4.5–9 $mg.kg^{-1}.h^{-1}$ and small incremental doses of fentanyl.

The dose-response part of the study was performed immediately following completion of induction of anaesthesia and determination of the supramaximal stimulation current. The fractional administration of Org 9426 was completed to a total of 300 $\mu g.kg^{-1}$, 2 min later followed by tracheal intubation. During the dose-response part of the study the patient's lungs were ventilated by mask. The end tidal $P\text{CO}_2$ was kept between 4.0 and 4.6 kPa.

Monitoring

In all patients the ECG, heart rate, end-tidal $P\text{CO}_2$ and O_2 saturation were monitored continuously. Blood pressure was measured every 3 min, and always just before and 2 min after administration of Org 9426.

Inspiratory and end-tidal concentrations of the volatile agents were measured continuously. Isometric measurement of the indirectly evoked twitch height was started after induction of anaesthesia. A peripheral nerve stimulator (Myotest, Biometer, Odense C., Denmark) was used and the ulnar nerve was stimulated at the wrist with supramaximal bipolar pulses of 0.2 ms duration via surface electrodes at a rate of 0.1 Hz (twitch response) or 2.0 Hz (train-of-four (TOF)), when appropriate. The resultant force of thumb adduction at a continuous preload of 200–400 g was quantitated with a force transducer/load cell (Statham UC3/UL4-20, Gould-Statham, Oxnard Ca, USA) with a baseline stabiliser (Muscle Relaxation Monitor, Anesthesiology Dept., University of Groningen, the Netherlands) and recorded on line (Astromed 102, West Warwick Atl., USA). During the measurements the oesophageal temperature was maintained at $\pm 37°C$ by means of a warming mattress and warmed inspired anaesthetic gases. The peripheral skin temperature of the arm was kept above 32.5°C. Monitoring of the neuromuscular response was continued until full recovery of the twitch height and a percentage TOF above 70% had been accomplished.

Experimental design

A schematic presentation of the study is shown in Figure 2.

The supramaximal stimulation current was determined after induction and stabilisation of anaesthesia and twitch height. Next, one of four selected initial doses of Org 9426 (120, 180, 240 or 300 $\mu g.kg^{-1}$) was administered in a randomised fashion. With each selected initial dose five patients were studied. Once the maximum effect of the selected initial dose was reached, i.e., when no further decrease in evoked twitch height occurred during three consecutive stimuli, a supplementary dose of Org 9426 (180, 120, 60, or 0 $\mu g.kg^{-1}$) was injected to reach a total dose of 300 $\mu g.kg^{-1}$ in all patients, This is approximately the ED_{90} dose for Org 9426 [2].

The onset time, clinical duration, duration of maintenance doses and recovery index were recorded. The onset time, defined as the time from the end of injection of the initial dose to the maximum effect, was measured in patients with a neuromuscular block between 5 and 95% of the control twitch height. The clinical duration, the time from the end of injection of the full initial dose of 300 $\mu g.kg^{-1}$ to 25% recovery of the twitch height, was measured. If necessary, maintenance doses of 150 $\mu g.kg^{-1}$ were administered at 25% recovery of the twitch height. The duration of the maintenance dose, defined as the time from the end of injection to 25% recovery of the twitch height, was recorded.

Following randomisation, in half of the patients the neuromuscular block was allowed to recover spontaneously and the TOF percentages were determined at 25%, 50%, 75% and 100% recovery of the twitch height. The remaining patients were given neostigmine methylsulphate 35 $\mu g.kg^{-1}$, to reverse the residual block at 25% of the

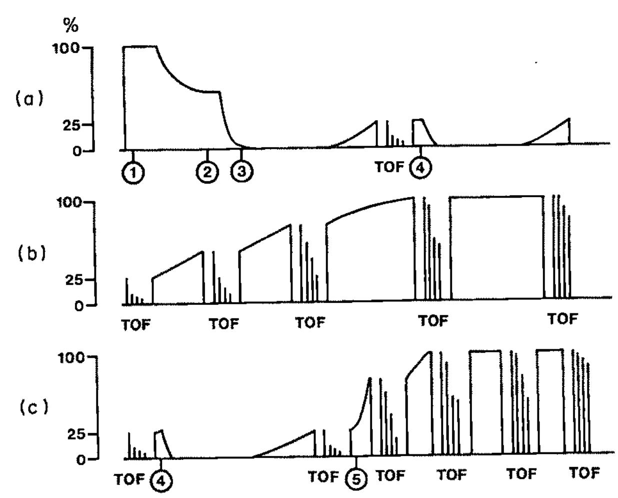

Fig. 2. Experimental procedure (schematic presentation). Vertical scale: control twitch height (%), horizontal scales: time. Upper (a) and middle (b) panels represent the dose-response part of the study with spontaneous recovery of Org 9426-induced neuromuscular blockade. Upper (a) and lower (c) panels demonstrate the procedure when the residual block was reversed with neostigmine. At point 1 the selected initial dose of Org 9426 and at point 2 a supplementary dose up to a total of 300 $\mu g.kg^{-1}$ were administered. At point 3 intubation was performed and at point 4 a maintenance dose of 150 $\mu g.kg^{-1}$ of Org 9426 was administered. At point 5 neostigmine was injected. Percentage train-of-four (TOF) was measured at 25, 75, 90 and 100% recovery of the twitch height (upper and middle panel) or 2, 5, 8 and 10 minutes after the administration of the reversal agent when recovery was induced (lower panel).

recovery of the twitch height. Methylatropine nitrate 7 $\mu g.kg^{-1}$ was administered simultaneously. Just before and 2, 5, 8 and 10 min after administration of the reversal agent, TOF percentages were determined. The recovery index, defined as the time between 25% and 75% recovery of the twitch height, was determined in all patients. From the above mentioned experimental procedure data could be generated for: construction of the dose-response curve by recording the maximum effect of the selected initial doses in all patients; measurement of the time course of action and reversibility of the effect of Org 9426 under the various anaesthetic techniques.

Statistical analysis

The dose-response data were analysed with log-logit regression analysis. Zero and hundred percent block were included and expressed as logit values of -2 and $+2$, respectively. A Chi-square test was used to compare male/female distribution between the various groups. The applied MAC values of the volatile agents [6–8], age, degree of block and time course of neuromuscular blocking effects were analysed with the ANOVA test and, if necessary, followed by Mann–Whitney U tests with Bonferroni correction. All data are presented as mean values with the standard deviation in brackets unless otherwise stated. Statistical significance was inferred if $p < 0.05$.

Results

All values are presented as mean (standard deviation).

There were no statistical differences between the five groups with respect to male/female distribution and age.

Table 1. Magnitude of block following Org 9426, 300 $\mu g.kg^{-1}$, administered in one single bolus dose ($n = 5$ in each group) or in two divided doses ($n = 15$ in each group), in patients anaesthetised with nitrous oxide 65% in oxygen, and halothane, enflurane, isoflurane, droperidol/fentanyl or propofol/fentanyl. The results are presented as mean (SD).

Anaesthetic technique	Single dose* Block (%)	Divided doses* Block (%)
halothane	76.4 (17.6)	80.3 (20.8)
enflurane	87.4 (12.7)	77.9 (23.2)
isoflurane	78.8 (19.1)	89.4 (14.6)
droperidol/fentanyl	84.8 (5.0)	70.9 (13.7)
propofol/fentanyl	80.6 (20.1)	77.7 (19.7)

*no significant differences between the percentages block between the various groups.

The degree of neuromuscular block was not significantly different between the various groups after the initial total dose of 300 $\mu g.kg^{-1}$ (Table 1). After 30 min at steady state anaesthesia the mean end-expiratory concentrations of the anaesthetics in oxygen/nitrous oxide 1/2 were 2.5 (0.5), 2.2 (0.5), and 2.7 (0.6) MAC for the halothane, enflurane, and isoflurane groups, respectively, in accordance with the MAC values mentioned in the literature [6–8].

Dose-response relationship

Log-logit linear regression analysis from the single bolus dose-response data revealed the following regression equation:

$$Y = 4.54\ X - 10.46,\ R = 0.7306$$

The ED_{50} and ED_{90} derived from this equation are 202 and 328 $\mu g.kg^{-1}$, respectively. The neuromuscular blocking effects of the 300 $\mu g.kg^{-1}$ dose of Org 9426, administered either as single bolus or in two fractions, are listed in Table 1. The mean value of twitch height depression after a total of 300 $\mu g.kg^{-1}$ Org 9426 amounted to 79.8% in all 100 patients.

Time course of action

The onset times after a bolus of 300 $\mu g.kg^{-1}$ of Org 9426 were 3.2 (0.8), 4.0 (0.0), 4.3 (2.0), 3.8 (1.3), and 3.4 (0.4) min for the halothane, enflurane, isoflurane, droperidol/fentanyl and propofol/fentanyl groups, respectively. These values are not significantly different.

The clinical duration of the total dose of 300 $\mu g.kg^{-1}$ of Org 9426 was 11 (5.7), 10.5 (5.9), 13.0 (6.5), 8.4 (2.5) and 8.8 (3.0) min in the halothane, enflurane, isoflurane, droperidol/fentanyl and propofol/fentanyl groups, respectively. All patients who received at least five times a maintenance dose of 150 $\mu g.kg^{-1}$ were compared with respect to the duration in Table 2.

No further increase in the duration of the maintenance doses were seen after 4–5 maintenance doses. The last TOF response at 25% of recovery in the isoflurane group (19.7 (9.6)%) did not differ from that in the enflurane group (12.6 (7.2)%), but was significantly higher than the values in the halothane, droperidol/fentanyl and propofol/fentanyl groups (7.8 (7.1), 7.8 (6.6), and 10.3 (6.3)%, respectively). The recovery indices did not significantly differ and were 16.7 (7.9), 16.2 (7.7), 11.9 (3.6), 9.5 (2.9) and 9.7 (3.2) min for the halothane, enflurane, isoflurane, droperidol/fentanyl and propofol/fentanyl groups, respectively. The TOF responses at 25%, 75%, 90% and 100% during spontaneous recovery are presented in Table 3.

Table 2. Duration of maintenance doses of Org 9426, 150 $\mu g.kg^{-1}$, in patients anaesthetised with nitrous oxide 65% in oxygen, and halothane, enflurane, isoflurane, droperidol/fentanyl or propofol/fentanyl, who received at least five maintenance doses. The results are presented as mean (SD).

Anaesthetic technique	*n*	Duration maintenance dose (min)				
		1	2	3	4	5
halothane	5	12.0 (3.1)	13.7 (3.6)	13.7 (3.1)	15.5 (2.7)	15.5 (3.2)
enflurane	7	12.5 (2.6)	14.8 (2.8)	15.9 (3.4)	17.4 (3.8)	18.9 (4.3)
isoflurane	8	13.4 (3.7)	14.6 (3.6)	16.2 (3.5)	18.3 (4.6)	18.1 (5.8)
droperidol/fentanyl	11	11.5 (2.6)	13.4 (2.2)	15.3 (4.0)	15.7 (3.6)	15.3 (3.9)
propofol/fentanyl	10	9.5 (1.9)	11.4 (2.6)	12.9 (3.2)	12.5 (3.1)	12.8 (3.5)

Table 3. Percentage recovery of the train-of-four (TOF) measured during spontaneous recovery of the twitch height in patients anaesthetised with nitrous oxide 65% in oxygen, and halothane, enflurane, isoflurane, droperidol/fentanyl or propofol/fentanyl. The results are presented as mean (SD).

		Percentage recovery of twitch height			
Anaesthetic technique	*n*	25	75	90	100
halothane	10	4.3 (4.0)	32.3 (20.1)	45.5 (16.7)	62.7 (21.9)
enflurane	10	11.7 (7.8)	33.1 (10.4)	44.8 (14.1)	43.3 (8.3)
isoflurane	9	14.8 (8.6)	37.8 (14.0)	47.0 (14.0)	53.3 (15.1)
droperidol/fentanyl	10	7.6 (6.6)	29.9 (13.0)	41.4 (20.0)	39.8 (14.6)
propofol/fentanyl	11	8.8 (4.2)	30.1 (11.9)	41.1 (17.0)	50.2 (16.7)

Table 4. Percentage recovery of the train-of-four (TOF) measured just before and at 2, 5, and 8 min after reversal with neostigmine, 35 μg.kg^{-1}, administered at 25% of recovery of the twitch height in patients anaesthetised with nitrous oxide 65% in oxygen, and halothane, enflurane, isoflurane, droperidol/fentanyl or propofol/fentanyl. The results are presented as mean (SD).

		Time after reversal (min)			
Anaesthetic technique	*n*	0	2	5	8
halothane	10	8.9 (8.2)	37.9 (12.1)	65.3 (5.0)	74.9 (3.9)
enflurane	10	12.9 (7.2)	31.6 (12.1)	57.7 (6.0)	74.7 (6.3)
isoflurane	9	22.3 (9.6)	53.7 (8.5)	69.8 (11.1)	75.3 (8.2)
droperidol/fentanyl	10	8.1 (7.5)	35.7 (11.1)	64.7 (8.1)	77.8 (8.1)
propofol/fentanyl	9	12.0 (7.9)	52.6 (15.0)	74.3 (10.4)	82.1 (4.7)

Table 5. Percentage change of heart rate and systolic and diastolic blood pressure following administration of maintenance doses of Org 9426, 150 μg.kg^{-1}, in patients anaesthetised with nitrous oxide 65% in oxygen, and halothane, enflurane, isoflurane, droperidol/fentanyl or propofol/fentanyl.

Anaesthetic technique	Number of doses	Heart rate	Systolic blood pressure	Diastolic blood pressure
halothane	72	+1.0	+0.7	+0.2
enflurane	62	+1.1	−0.5	+0.3
isoflurane	63	+0.8	+1.2	0
droperidol/fentanyl	108	−2.1	−1.8	−1.5
propofol/fentanyl	96	+1.0	+0.1	+1.3

Reversal of the residual neuromuscular block was easily accomplished. The recovery indices after neostigmine were 3.1 (0.8), 3.2 (1.3), 2.3 (1.1), 3.3 (1.1) and 2.1 (0.9) min for the halothane, enflurane, isoflurane, droperidol/fentanyl and propofol/fentanyl groups, respectively. These values are not significantly different. The TOF exceeded the TOF value of 70% in all groups within eight minutes following the administration of the reversal agent (Table 4).

Cardiovascular and other effects

No significant changes in heart rate and blood pressure under stable anaesthetic conditions, i.e., following maintenance doses, were recorded. The data are presented in Table 5. No local or general side effects were observed.

Discussion

This study was designed to provide the clinician with useful data for clinical application of Org 9426. Therefore, we allowed only a small delay after induction of anaesthesia to determine the supramaximal stimulation and to stabilise twitch height before injecting Org 9426 (3–5 min). We did not include a period of equilibration of the volatile anaesthetics, since administration of the neuromuscular blocking agent in daily clinical practice usually precedes or immediately follows the administration of the volatile anaesthetic. The expected differences in dose-response relationship between the various anaesthetic groups under the experimental conditions of the study have been shown to be limited and not significant [9]. Hence, an overall regression analysis of all dose-response data seems to be justified. A small number of 0 and 100% responders were included in the construction of the curve, using the logit values as stated in the methods in order to get a better estimate of the true population mean [10]. The resulting ED_{90} dose of Org 9426 of 328 μg.kg^{-1} accords with results of other studies [1, 2], indicating a potency ratio of Org 9426 as compared to vecuronium of 6 to 7. When the degree of block in the various anaesthetic groups after a bolus of 300 μg.kg^{-1} of Org 9426 (Table 1) is compared, only small, non-significant differences in the degree of block exist between the five anaesthetic groups. The onset time of subtotal paralysing doses of Org 9426 (3–4 min), i.e., doses resulting in a twitch

depression between 5 and 95%, is considerably shorter than that of other neuromuscular blocking drugs with an intermediate duration of action, such as vecuronium (6–7 min) [11] and atracurium (6–7 min) [12]. The main differences in onset of neuromuscular block are the shorter lag time, i.e., the time between end of injection and the first detectable decrease of the twitch, and the faster initial rate of block development of Org 9426 [2].

In this study the potentiation of the volatile anaesthetic could best be evaluated from the duration of the maintenance doses, when the concentration of the anaesthetic in the biophase is assumed to approach an equilibrium with measured end-expiratory concentrations. In this investigation we titrated the volatile anaesthetic to the need of the patient. The calculated mean value of MAC at 30 min following induction were not significantly different between the three groups [6–8].

The slight increase of the duration of maintenance doses, which only occurred in the first 1.5 h, may be regarded as the consequence of administration of low initial doses of Org 9426, even less than the ED_{90} dose, which will delay the saturation of the distribution compartment. Most probably the temporary increase in the duration of the maintenance doses will be absent following a higher initial dose, i.e., an intubating dose of Org 9426. In this study design, stabilisation of the duration of maintenance doses was probably due to both achieving equilibrium of Org 9426 between the central and the distribution compartment and completion of the wash-in of the volatile anaesthetics in the biophase.

There was a tendency towards a longer duration of action of Org 9426 in the enflurane and isoflurane groups. However, the extent of prolongation in the isoflurane and enflurane as compared with the halothane, droperidol/fentanyl and propofol/fentanyl groups ($\pm 25\%$), appeared to be negligible due to the wide range in individual responses within the separate groups.

The recovery indices and the rate of TOF recovery in the absence or presence of neostigmine are similar to values after vecuronium or atracurium [13–15]. The tendency to a shorter recovery index and a significantly more favourable TOF response at 25% of recovery of control twitch height in the isoflurane group compared to halothane, droperidol/fentanyl and propofol/fentanyl groups may be the result of a greater contribution of the anaesthetic agent to the degree of block. This, in turn, may facilitate reversal since a relatively lower concentration of the neuromuscular blocking agent will be present in the biophase. Concentration-response studies under various anaesthetic techniques are needed to confirm this assumption.

Under relatively stable anaesthetic conditions Org 9426 showed cardiovascular stability, however, it should be realized that the cardiovascular effects were evaluated using relatively small doses of Org 9426.

We conclude that Org 9426 is a non-depolarising neuromuscular blocking agent of an intermediate duration of action. Its time course of neuromuscular blocking action is only slightly influenced by the anaesthetic techniques employed in this study. Org 9426 can be readily reversed by neostigmine and appears free from side effects in the doses used in this and earlier studies [1,2]. Org 9426 may, therefore, be characterised as a vecuronium-like agent with a reasonable potency and a significantly shorter onset time, mainly due to its more rapid initial onset of block.

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Effects of epidural diamorphine on the somatosensory evoked potential to posterior tibial nerve stimulation

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Summary

We have studied the effects of the epidural administration of diamorphine 0.1 mg/kg at the L_{3-4} interspace on somatosensory evoked potentials in the cervical epidural space before corrective surgery for idiopathic adolescent scoliosis. A further eight patients in whom anaesthesia was maintained with a propofol infusion acted as a control group. Epidural diamorphine had no effect on the latency or amplitude of the evoked potentials. We conclude that epidural diamorphine is a suitable technique to use in scoliosis surgery because of its lack of effect on neurophysiological variables, although the potential respiratory problems need investigation.

Key words

Anaesthetic techniques, regional; epidural
Analgesics; diamorphine.
Monitoring; somatosensory evoked potentials.

Somatosensory evoked potentials (SEP) measured in the epidural space are commonly used to provide information about spinal cord integrity during scoliosis surgery[1] and have been shown to be affected minimally by volatile anaesthetic agents.[2,3] The effects of the epidural administration of local anaesthetic agents and opioids on cortically recorded SEPs have been investigated,[4,5] but there are few data about the action of these drugs on the epidural SEP.

We have shown recently that the epidural administration of 2% lignocaine 10 ml at the L_{3-4} interspace resulted in a significant decrease in the overall amplitude, and the amplitude of the later peaks, of the epidural SEP to posterior tibial nerve stimulation.[6] We advised caution, therefore, in the use of epidural 2% lignocaine for scoliosis surgery because it may interfere with the intra-operative monitoring of the SEP. The alleviation of severe postoperative pain is an essential component of anaesthesia for scoliosis surgery and this could be provided by the use of epidural opioids. In the present study we have examined the effects of the epidural administration of diamorphine 0.1 mg/kg body weight on the SEP to posterior tibial nerve stimulation to assess its suitability for scoliosis surgery.

Methods

We studied 16 patients admitted to the Royal National Orthopaedic Hospital for corrective surgery for idiopathic adolescent scoliosis. The study was approved by the Hospital Ethics Committee and written, informed consent was obtained from the patients, or parents, as appropriate.

All patients were premedicated with intramuscular papaveretum 0.3 mg/kg and hyoscine 0.006 mg/kg 90 minutes before induction of anaesthesia. Anaesthesia was induced with propofol 2.5 mg/kg and tracheal intubation facilitated with pancuronium 0.08 mg/kg. The lungs were ventilated with 70% nitrous oxide in oxygen and a radial artery cannulated for the measurement of arterial pressure. The patients were placed in a prone position on a Montreal mattress and a recording electrode was inserted into the epidural space at the C_7–T_1 interspace. Baseline recordings of the epidural SEP to posterior tibial nerve stimulation of each limb were obtained. Full details of the methods of nerve stimulation and measurement of the cervical epidural SEP have been described previously.[6]

The patients were allocated at random to two groups.

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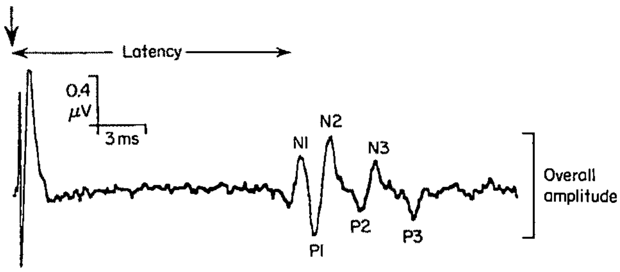

Fig. 1. Somatosensory evoked potential recorded in the cervical epidural space showing overall amplitude and first (N1P1), second (N2P2) and third (N3P3) peaks. First peak latency is measured from stimulus, shown by vertical arrow, to N1 peak.

One group ($n = 8$) received epidural diamorphine 0.1 mg/kg dissolved in 10 ml 0.9% sodium chloride solution at the L_{3-4} interspace while the remaining patients ($n = 8$) acted as a control group. A three-stage infusion of propofol was then started in all patients: 21 mg/kg/hour for 5 minutes, 12 mg/kg/hour for 10 minutes and 6 mg/kg/hour thereafter. This infusion regimen has been shown to result in stable blood concentrations of propofol 30 to 50 minutes after the start of the infusion.[7]

SEP measurements from the cervical epidural space to alternate posterior tibial nerve stimulation were made 30, 40 and 50 minutes after the epidural injection (diamorphine group) or start of infusion of propofol (control group). At each time point a minimum of three SEPs from each leg were recorded and the mean arterial pressure was measured. Ventilation was adjusted to maintain an end-tidal CO_2 concentration of 3.5–4.0% and the rectal temperature remained greater than 35°C. At the end of the study the patient was taken into the operating theatre and surgery commenced. The epidural electrode was then used to monitor the SEP during corrective surgery.

A typical SEP is shown in Fig. 1. The potentials were analysed for overall amplitude, peak-to-peak amplitude of the three peaks (N1P1, N2P2 and N3P3) and first peak latency. The identity of the patients was not known by the investigator analysing the SEPs. The results are presented as medians and ranges. Statistical evaluation was undertaken using the Wilcoxon signed rank test, Mann–Whitney *U* test and Spearman's rank correlation coefficient as appropriate.

Results

Mean (SEM) age and body weight were similar in the two groups: diamorphine 21.2 (1.9) years and 59.2 (13.1) kg and control 19.8 (1.8) years and 55.9 (7.3) kg.

The overall amplitude of the epidural SEP for the two groups is shown in Table 1. There was no significant change from baseline values within the groups and no significant difference between the groups. Similarly, there was no significant difference between the groups in first, second or third peak amplitude.

The first peak latency of the SEP for the two groups is shown in Table 2. Although latency increased during the study in both groups, this change was not statistically significant and there was no significant difference between the groups.

Mean arterial pressure decreased similarly in both groups during the propofol infusion. There was no significant correlation between the neurophysiological variables and mean arterial pressure.

Table 1. Median (range) overall amplitude of SEP (µV) in the epidural diamorphine and control groups. There was no significant difference between the groups during the study.

	Left leg		Right leg	
Time (minutes)	Diamorphine ($n = 8$)	Control ($n = 8$)	Diamorphine ($n = 8$)	Control ($n = 8$)
0	1.32 (0.51–1.95)	1.14 (0.71–2.78)	1.90 (0.95–2.58)	1.48 (0.63–1.81)
30	1.36 (0.64–2.06)	1.18 (0.69–2.65)	1.92 (0.92–2.67)	1.43 (0.66–2.09)
40	1.24 (0.63–2.16)	1.16 (0.68–2.61)	1.81 (0.88–2.75)	1.48 (0.63–2.10)
50	1.24 (0.67–2.09)	1.16 (0.64–2.57)	1.75 (0.89–2.70)	1.44 (0.65–2.09)

Table 2. Median (range) latency (ms) in the epidural diamorphine group and the control group. There were no significant differences between the groups during the study.

	Left leg		Right leg	
Time (minutes)	Diamorphine ($n = 8$)	Control ($n = 8$)	Diamorphine ($n = 8$)	Control ($n = 8$)
0	15.4 (15.0–19.9)	16.1 (14.0–16.9)	15.5 (14.4–20.1)	16.1 (14.9–17.8)
30	15.7 (15.1–20.0)	16.3 (14.3–16.9)	15.8 (14.4–20.3)	16.4 (15.1–16.8)
40	15.8 (14.4–20.1)	16.5 (14.5–19.3)	15.9 (13.6–20.3)	16.5 (15.3–19.3)
50	15.8 (14.8–20.1)	16.5 (14.6–19.5)	15.9 (14.1–20.3)	16.5 (16.3–19.4)

Discussion

We have shown that the administration of diamorphine 0.1 mg/kg in the lumbar epidural space does not result in a change in the cervical epidural SEP to posterior tibial nerve stimulation. In the only comparable study, to date, Lund and colleagues found that the cortically recorded SEP to electrical stimulation of the L_1 and S_1 dermatomes was not altered by the epidural administration of morphine 6 mg.[5] Although these workers did not study a control group, and the epidural recording electrode represents an improvement in the assessment of afferent neuronal conduction in the cord, our findings are similar. Lund and colleagues observed a small increase in latency after epidural morphine, but since both control and experimental groups showed a similar increase in this and other studies,[3,6] we do not consider this change in latency to be of importance.

The failure of epidural diamorphine to decrease the SEP may be due to several factors. First, the SEP recorded in the cervical epidural space is considered to represent afferent transmission in the anterolateral tracts (first peak) and dorsal columns (second and third peaks).[1,2] It should, therefore, reflect overall afferent sensory activity, but may not do so consistently under all clinical conditions. Secondly, there may have been insufficient diamorphine reaching the opiate receptors in the dorsal horn of the spinal cord after passage through the dura. It has been shown in an animal model that the direct application to the cord of morphine 0.1 mg is necessary to suppress neuronal activity in the dorsal horn.[8] Thus, the failure to find an effect of the opiate clinically, compared with the experimental data, could be a simple dose-related phenomenon.

Thirdly, it is probable that some noxious afferent activity arising after stimulation of the posterior tibial nerve bypasses the opiate receptors in the superficial laminae (I and II) of the dorsal horn.[9] Although C-fibres terminate mainly in lamina II, Aδ-fibres terminate in laminae I and V, so that rostral transmission can still occur in Aδ-fibres after the use of epidural opiates. A small proportion of C-fibres enter the cord via the ventral horn and also end in lamina V.[10] Fourthly, stimulation of the posterior tibial nerve activates not only Aδ- and C-fibres but also non-nociceptive fibres. This 'contamination' with nonnociceptive afferents is a common problem in all studies in which pain is assessed by evoked potentials,[11] and may have contributed to the maintenance of the SEP after diamorphine.

In conclusion, we have shown that lumbar epidural diamorphine 0.1 mg/kg has little effect on the SEP measured in the cervical epidural space. Epidural opioids can be recommended for use in scoliosis surgery because they do not interfere with intra-operative monitoring of spinal cord function. However, the possible depressive effects of epidural diamorphine on respiratory function in patients whose ventilation is compromised needs careful evaluation.

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Analgesic efficacy of controlled-release dihydrocodeine

A comparison of 60, 90 and 120 mg tablets in cold-induced pain

H. A. WOTHERSPOON, G. N. C. KENNY AND C. S. McARDLE

Summary

A prospective, double-blind, single-dose placebo-controlled four-part crossover study of 12 healthy volunteers was carried out to compare the analgesic efficacy of controlled-release dihydrocodeine tablets 60, 90 and 120 mg (DHC Continus tablets, Napp Laboratories) in cold-induced pain. Subjects received each of the four treatments in a random order using a latin square design. On each of the four study days, the volunteers performed cold pressor tests, before dose and again at 4, 8 and 12 hours after dose. Subjects rated their pain continuously over a 120-second period using a visual analogue scale. At 4 hours there was a significant reduction in pain in subjects who received 120 mg or 90 mg tablets compared with placebo, and in subjects who received 120 mg tablets compared with those who received 60 mg tablets. At 8 hours, 120 mg and 90 mg dihydrocodeine were still better than placebo. There was no significant difference in side effects between treatments.

Key words

Analgesics; dihydrocodeine.
Pain; cold-induced.

Dihydrocodeine is an opioid analgesic which has been shown to be effective in the treatment of moderately severe pain.[1-3] Until recently, it was only available in injectable form or as a normal release tablet formulation. In 1988 a new controlled-release oral preparation of dihydrocodeine 60 mg, designed for twice daily dosing, was developed.

The analgesic efficacy of controlled-release dihydrocodeine 60 mg tablets and normal release dihydrocodeine 30 mg tablets was examined in patients with chronic back pain and in patients with osteoarthritis of the weight-bearing joints. This study demonstrated that controlled-release dihydrocodeine 60 mg tablets administered twice daily was as effective as the normal release preparation given as 30 mg four times daily.[4] The efficacy of controlled-release dihydrocodeine 60 mg in comparison with normal release dihydrocodeine 30 mg was further evaluated in 90 patients following sternotomy. A patient-controlled analgesia system was used to supplement the dihydrocodeine, and morphine requirements were significantly reduced with both active preparations compared to placebo.[5]

Further to this work, controlled-release dihydrocodeine tablets 90 mg and 120 mg have been developed for evaluation. The aim of this study was to assess the relative analgesic efficacy of controlled-release dihydrocodeine 60, 90 and 120 mg compared with placebo using cold-induced pain[6] in healthy volunteers.

Methods

Healthy male volunteers aged between 18 and 40 years who had undergone preliminary screening (including history, physical examination, haematological and biochemistry testing, 12-lead ECG recording and narcotic screening) were entered into the study. Subjects with a history of sensitivity to dihydrocodeine, chronic alcohol abuse or those known to smoke were excluded. Subjects who had taken prescribed medication within the 4 weeks before the study or any 'over the counter' medication within 48 hours of the start of the study were not eligible.

In order to familiarise subjects with the cold-pressor test, a minimum of four training sessions were completed, two sessions on each occasion, separated by approximately 3 days. All tests were performed with the subjects sitting in a quiet room with no external interferences. Room temperature was kept at 20°C (SD 2°C). There were no clocks in the room and no wrist watches were allowed.

Subjects placed their non-dominant hand up to the ulnar prominence in a thermostatically controlled water bath at 37°C$\pm$1°C. After 2 minutes, they transferred their hand into a water bath at 3°C$\pm$0.5°C. Over the next 120 seconds they rated their pain continuously using a hand-controlled paddle linked to a visual analogue scale (VAS) displayed on a computer monitor. The scale ran from 0 to

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10 where 0 corresponded to no pain and 10 represented maximum pain. The VAS pain scores, recorded at 2-second intervals over the 120-second period, were stored on computer disk. After 120 seconds, they removed their hand from the water.

Successive cold pressor tests were checked for reproducibility and, if necessary, further tests were carried out until readings were consistent. A maximum of eight training sessions per subject were permitted. Those who demonstrated reproducible baseline pain values were entered into the study, commencing 3–10 days after the last training session

Subjects were instructed to fast from 2300 hours on the previous day, abstain from any methylxanthine-containing foods and drinks such as tea, coffee, cola and chocolate for 12 hours and abstain from alcohol for 24 hours before each study. During each study day, subjects received a standard lunch 4 hours after the test medication had been administered and a standard dinner 6 hours later.

Subjects were allocated to receive the four treatments (placebo, 60 mg, 90 mg, 120 mg) in a random order using a latin square design to control for order effects. Each treatment period consisted of one day with a minimum of 3 days and a maximum of 10 days between treatments. In order to maintain the double-blind design of the study, subjects were given one tablet of the test medication and matching placebo tablets of the two alternative strengths (or placebos of all three) at approximately 0900 hours on each of the four study days (Table 1). On each day four cold pressor tests were carried out; the initial test was performed before ingestion of the tablets and then repeated at 4, 8 and 12 hours. Volunteered symptoms and side effects were documented before each test.

The pain scores recorded at 0, 4, 8 and 12 hours after treatment were compared using the area under the pain score versus time curve (AUC). The AUC values up to 2 minutes were compared to give an indication of the total amount of pain experienced by the volunteer during the cold pressor test.

Before medication the AUC values varied from day to day. To compensate for this, the analysis was carried out on the ratio of the AUC to the baseline (0 hours) for each treatment. Repeated measures analysis of variance was used to detect any treatment effects on the AUC ratio. The least significant difference method was used to compare the mean AUC ratio for any two treatments. The least significant difference is the smallest difference between any two treatment means that would be statistically significant when one adjusts for the multiple comparisons involved. Fisher's exact test was used to compare the frequency of reporting side effects of the two extreme treatments (placebo and 120 mg tablets) and if a difference was seen, the other pairs were compared. All statistical tests were carried out at the 5% significance level.

Table 1. Treatment administration.

Group	60 mg	90 mg	120 mg
60 mg	Active	Placebo	Placebo
90 mg	Placebo	Active	Placebo
120 mg	Placebo	Placebo	Active
Placebo	Placebo	Placebo	Placebo

Table 2. Ratio of the area under pain score versus time curve (AUCratio) 4 hours after dose.

Treatment	*n*	Mean	SD
Placebo	12	96.1	8.64
DHC 60 mg	12	89.3	14.04
DHC 90 mg	12	86.6	12.30
DHC 120 mg	12	78.4	18.32

The least significant difference was 9.2, so that the following comparisons were statistically significant: DHC 120 mg vs placebo; DHC 120 mg vs DHC 60 mg; DHC 90 mg vs placebo.

Table 3. Ratio of the area under pain score versus time curve (AUCratio) 8 hours after dose.

Treatment	*n*	Mean	SD
Placebo	12	99.3	17.70
DHC 60 mg	12	89.2	15.10
DHC 90 mg	12	83.4	11.83
DHC 120 mg	12	82.7	19.83

The least significant difference was 11.7, so that the following comparisons were statistically significant: DHC 120 mg vs placebo; DHC 90 mg vs placebo.

Table 4. Ratio of the area under pain score versus time curve (AUCratio) 12 hours after dose.

Treatment	*n*	Mean	SD
Placebo	12	95.1	26.54
DHC 60 mg	12	87.3	14.90
DHC 90 mg	12	91.7	18.92
DHC 120 mg	12	87.4	14.60

The least significant difference was 11.4, so that no significant treatment effects were observed.

Results

Thirteen subjects were eligible for the study, but one volunteer withdrew after two training sessions. Twelve volunteers, therefore, completed the study.

The mean AUC ratio and standard deviation of each treatment group at 4 hours after treatment are shown in Table 2. The AUC ratio for both the 90 mg and 120 mg tablets was significantly different to that of placebo. In addition, the AUC ratio for the 120 mg tablets was significantly different to that of the 60 mg tablets. At 8 hours after treatment the AUC ratio for both the 90 mg and 120 mg tablets was again significantly different to that of the placebo (Table 3). At 12 hours after treatment no significant treatment difference was observed (Table 4). Drowsiness and headache were the most frequently reported side effects, but the difference between 120 mg tablets and placebo was not significant for either symptom.

Discussion

In the assessment of analgesics, experimental models applying a painful stimulus to healthy volunteers have proved to be of value. Furthermore, the laboratory environment facilitates the study of the dose–effect relationship using a crossover design under controlled, double-blind conditions.[7] The cold pressor test[6,8–10] has

proven sensitivity and has previously demonstrated variations between different analgesics and, indeed, between different strengths of analgesics.[11] In this study we used the cold pressor test to assess the relative analgesic efficacy of three strengths of controlled-release dihydrocodeine tablets (60 mg, 90 mg and 120 mg) compared with placebo tablets.

The time for controlled release dihydrocodeine 60 mg and 120 mg to reach peak serum levels is 4 hours.[14] At 4 hours and 8 hours after administration of the study medication a clear difference in the AUC ratios was observed between all three strengths of controlled-release dihydrocodeine and placebo; the differences between 120 mg and placebo and 90 mg and placebo were significant. At 4 hours, the difference between 120 mg and 60 mg was also significant. At 12 hours after treatment all three strengths of controlled-release dihydrocodeine decreased the total pain experienced by the volunteers but no significant differences were seen between strengths.

Drowsiness and headache were the most common of the side effects reported. The majority of all the reported side effects were classified as mild in nature. There was a higher frequency of drowsiness and headache after administration of controlled-release dihydrocodeine 120 mg compared to the two lower strengths of dihydrocodeine and placebo, although this was not statistically significant.

In conclusion, this study has shown that there was a clear dose–response relationship between controlled-release dihydrocodeine 60 mg, 90 mg and 120 mg; proportionately greater analgesia was obtained with the 90-mg and 120-mg strengths compared to the 60-mg tablet. These results confirm that controlled-release dihydrocodeine 90 mg and 120 mg are effective analgesics in the control of severe pain.

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Pain following thoracotomy

A randomised, double-blind comparison of lumbar versus thoracic epidural fentanyl

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Summary

Fifty-eight patients scheduled for elective thoracotomy were randomly allocated to receive fentanyl by either the thoracic or the lumbar epidural route for postoperative analgesia. The infusion rate was adjusted to optimise analgesia. Dose adjustment, pain assessment and the incidence of side effects were monitored by a blinded observer at set times over the 24 hour study period. Similar pain scores were obtained in both groups at all assessment times. In addition, there was no significant difference in dose requirements or incidence of side effects between the two groups. There appears little justification for the use of the generally less familiar, and potentially more dangerous, thoracic approach when fentanyl alone is infused into the epidural space following thoracotomy.

Key words

Anaesthetic techniques, regional; epidural.
Pain; postoperative.

Opioids administered by the epidural route are widely used in the management of postoperative pain.[1] The quality of analgesia achieved is superior to that of intramuscular administration and permits improvements in both postoperative respiratory performance and compliance with physiotherapy.[2,3] This is particularly beneficial following thoracotomy, when pulmonary function may already be severely compromised.

Morphine has been the opioid most commonly administered by the epidural route; it is relatively hydrophilic and is poorly absorbed by neural tissue of the spinal cord. Thus, once spread of the drug across the dura has occurred, the persistence of high concentrations of morphine in the cerebrospinal fluid (CSF) promotes rostral spread. Whilst this may be beneficial for incisions within the thoracic dermatomes,[4] further spread may involve the brainstem with the potential for delayed respiratory depression.[5]

In order to reduce this potential problem, the more lipophilic opioids, such as fentanyl and diamorphine, have been studied. The rapid uptake of these drugs by spinal cord tissue should reduce their concentration in the CSF, and theoretically limit rostral spread. The implication of this rapid uptake of fentanyl into the spinal cord is that the drug may have a 'segmental' effect. Following thoracotomy, this would require the placement of the epidural catheter in the thoracic region, and there have been a number of studies using thoracic epidural fentanyl following thoracotomy.[6,7]

Recently, the potential dangers of thoracic epidural cannulation have been stressed,[8] the most important of which is damage to the spinal cord. The spinal cord in an adult ends at the level of the T_{12}–L_1 vertebrae, and hence lumbar epidural cannulation is not associated with this potential problem; in addition it is generally considered to be technically easier than the thoracic route. A recent study by Melendez *et al.*[9] has suggested that fentanyl administration by the lumbar epidural route may be effective for post-thoracotomy pain. The aim of this study was to determine whether infusing fentanyl through an epidural catheter inserted at the level of the incisional dermatome conferred any clinical advantage over the much safer and more familiar lumbar route.

Methods

The study was approved by the Hospital Ethics Committee and informed consent was obtained from all patients. Patients scheduled for elective thoracotomy were randomly

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Table 1. Verbal ranking score.

Pain score	Pain experience
0	No pain on deep inspiration
1	Pain only on deep inspiration (i.e. no pain on tidal breathing)
2	Pain on tidal breathing: mild
3	Pain on tidal breathing: moderate
4	Pain on tidal breathing: severe

allocated to have either thoracic (group T) or lumbar (group L) epidural catheters inserted. In all patients surgery was performed through either the right or left sixth intercostal space.

Patients were premedicated with oral diazepam 10–20 mg according to size and age. Epidural catheters were inserted under full aseptic conditions using the loss of resistance technique; thoracic catheters were inserted at T_{6-8} and lumbar catheters at L_{2-3} level. Correct placement was confirmed by the catheter advancement test,[10] leaving 3–4 cm in the epidural space. An antibacterial filter was attached to the catheter and the entire lumbar and thoracic area covered with an opaque waterproof dressing.

Anaesthesia and muscle relaxation were induced with thiopentone 3–5 mg/kg, vecuronium 0.15 mg/kg and maintained with nitrous oxide, oxygen and isoflurane. The inspired oxygen concentration was adjusted to maintain a haemoglobin saturation of at least 95% during one-lung ventilation. A single intravenous dose of fentanyl 3 μg/kg (maximum dose of 200 μg) was administered prior to skin incision.

Epidural fentanyl infusions were prepared in a concentration of 10 μg/ml in normal saline.[7] An initial loading dose of 1.5 μg/kg was administered approximately 1 hour before the end of the procedure and was followed by an infusion rate of 0.4 μg/kg/hour. At the end of surgery all patients were extubated and returned to the postoperative care area.

Pain assessment was performed at 2, 4, 8, 16 and 24 hours postoperatively using a standard 10 cm visual analogue scale (VAS), ranging from no pain to the worst pain imaginable. In addition, a verbal ranking score (VRS) was used (Table 1).

The epidural infusion rate was adjusted to achieve the best analgesia possible; a VRS of one or less was sought. If the initial infusion was inadequate in this respect, a further loading dose of 1 μg/kg was administered and the rate increased in increments of 0.2 μg/kg/hour to a maximum of 1.4 μg/kg/hour. The rate was reduced by 0.2 μg/kg/hour if there were two consecutive satisfactory VRS scores. No other opioids were administered during the period of epidural infusion. A period of at least 30 minutes was allowed between dose adjustments. Heart rate, blood pressure and respiratory frequency were monitored hourly during the study period.

Table 2. Demographic data.

	Thoracic (Group T) $n = 28$		Lumbar (Group L) $n = 24$	
Age; years	Mean	62.3	Mean	61.8
	Median	66	Median	61
	Range	16–82	Range	41–81
Sex; M/F	21/7		15/9	
Weight; kg	Mean	65.2	Mean	71*
	Median	62	Median	68
	Range	40–95	Range	51–107

*$p < 0.05$.

Table 3. Details of surgical procedure.

	Thoracic epidural $n = 28$	Lumbar epidural $n = 24$
Oesophagogastrectomy	9	6
Hiatus hernia repair	3	4
Pneumonectomy	4	5
Lobectomy	4	5
Wedge resection	5	3
Bullectomy	1	0
Decortication	1	0
Pleurectomy	1	1

At the end of each pain assessment, patients were asked about nausea, itching and urinary retention. Dose adjustment, pain assessment and the recording of adverse effects were performed by one of the authors who was blind to the position of the catheter and otherwise uninvolved in the perioperative management of the patient.

Statistical analysis

The pain scores were analysed using the Mann–Whitney *U* test. The incidence of side effects was compared by the Chi squared test as appropriate. A p value of less than 0.05 was taken to be significant.

Results

Fifty-eight patients were studied and the two groups were similar with regard to age and sex (Table 2), but the mean weight was significantly higher in the lumbar epidural group ($p = 0.03$).

Six patients were removed from the study, four in the thoracic group and two in the lumbar group. There were two failures to locate the epidural space (both in the thoracic group), and two departures from protocol. One patient had an undiagnosed phaeochromocytoma and a further patient was withdrawn due to intractable nausea. The type of operation performed is shown in Table 3.

The VAS and VRS scores are shown in Figures 1 and 2. The verbal ranking results showed very similar pain ranking between the two groups, demonstrating that target analgesia was generally achieved. With analogue pain scoring, the lumbar group appeared to have higher mean pain scores at all measurement periods, particularly in the first 2 hours. However, these differences did not reach statistical significance. The mean number of bolus doses received by the groups was also similar (T = 0.95 (range 0–3) L = 1.3 (range 0–3)).

The total fentanyl requirement over the 24 hour study period and the mean fentanyl infusion rate (μg/kg/hour) are shown in Table 4. The lumbar group received significantly more fentanyl ($p = 0.03$). However, fentanyl was infused on a weight basis and the lumbar group was

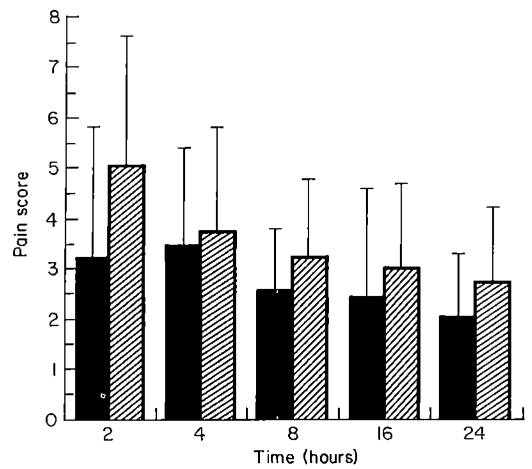

Fig. 1. Bar chart showing the mean (SD) visual analogue pain scores at fixed measurement intervals following thoracotomy. ■ thoracic epidural; ▨ lumbar epidural.

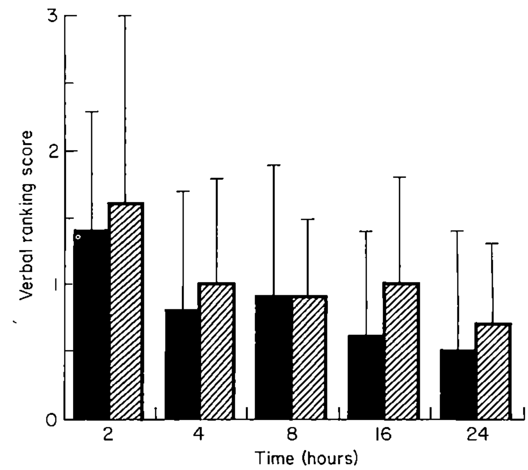

Fig. 2. Bar chart showing the mean (SD) verbal ranking pain scores following thoracic and lumbar epidural fentanyl for thoracotomy pain. ■ thoracic epidural; ▨ lumbar epidural.

significantly heavier than the thoracic group. When the dose requirement was analysed as μg/kg/hour there was no significant difference between the two groups.

The incidence of urinary retention, nausea and pruritus are shown in Table 5. The incidence of retention in patients not catheterised as part of the procedure was higher in the lumbar group. This difference did not reach statistical significance.

Nausea proved intractable in one patient in the thoracic group and she was therefore withdrawn from the study. Her results were not included in the analysis of pain scores and dose requirements.

Pruritus occurred in seven patients but appeared to be a minor problem requiring no treatment. There were no episodes of delayed respiratory depression.

Discussion

One of the difficulties inherent in a study of this kind is the selection of a suitable and repeatable endpoint of analgesic effect. One approach to the problem has been the selection of a specific and necessarily arbitrary endpoint on a visual analogue scale.[11] We feel that the use of our verbal ranking score allows a more objective and comparable endpoint. The absence of pain during normal tidal breathing (VRS 0–1) was felt to be a realistic endpoint for the use of epidural opioids alone. Whilst analgesia during deep inspiration was achieved in a number of our patients towards the end of the study period, this would only be a realistic endpoint for the majority if there was concurrent use of local anaesthetics applied to the segmental level of the incision.

Table 4. Fentanyl requirement in the first 24 hours of study.

	Thoracic epidural	Lumbar epidural
Total fentanyl requirement; μg, mean (SD)	974 (371)	1161 (267)*
Infusion rate; μg/kg/hour, mean (SD)	0.57 (0.14)	0.69 (0.18)

*p = 0.03.

In starting with a low infusion rate, combined with frequent assessment and dose adjustment, the study was designed to establish the minimum effective infusion rate. This may be responsible for the relatively high pain scores during the first 2 postoperative hours when most of the adjustments in infusion rate occurred. In trying to define the minimum effective dose we hoped both to reduce the incidence of side effects and to demonstrate any small differences in fentanyl requirement between the two routes of administration. It may also account for the relatively low mean fentanyl requirement compared with other studies; in a comparative study with intramuscular papaveretum, Welchew *et al.*[7] used a fixed infusion rate of 0.85 μg/kg/hour through an epidural catheter in the thoracic position.

One other study has attempted to address the question of a segmental effect of epidural fentanyl following thoracotomy.[12] With the dose adjustment titrated by both the anaesthetist and a patient demand system, Chamberlain *et al.* demonstrated that thoracic administration resulted in pain scores that were significantly better than lumbar administration ($p < 0.001$). However, there is now increasing evidence that intravenous absorption of fentanyl is responsible for a significant component of the analgesia achieved by epidural administration;[13,14] indeed the plasma opioid level may be identical to that achieved following direct intravenous infusion.[11] As the vascularity of the epidural space is unlikely to vary markedly from the thoracic to lumbar region, similar absorption would be likely in both groups, tending to mask any effects due purely to a segmental action. It is surprising, therefore, that

Table 5. Incidence of side effects.

	Thoracic epidural $n = 28$	Lumbar epidural $n = 24$
Retention of urine requiring catheterisation	1	4
(Number of patients catheterised as part of procedure)	9	6
Nausea and vomiting	4	3
Pruritus	3	4

Chamberlain and colleagues were able to demonstrate a segmental effect with such a high degree of statistical significance using a sample size of only 10 patients in each group.

In our study, epidural fentanyl was well tolerated with few side effects in either group. Only one patient developed nausea that required discontinuation of the infusion, and the incidence of pruritus was so low as to be discounted as a significant side effect. This is in marked contrast to studies of epidural opioids in other types of surgery. Following Caesarean section, Ellis *et al.* [14] noted that 38% of patients required diphenhydramine for intractable itching. The dose infused in that study (1.88 (SD 0.4) μg/kg/min) was much higher than that used in our study. However, it is uncertain whether pruritus is dose- or age-related and indeed it has been suggested that parturients may be particularly susceptible to the pruritic effects of spinal narcotics.[15]

This study further confirms the excellent analgesia provided by epidural fentanyl following thoracotomy. Both lumbar and thoracic administration have similar analgesic effects, dose requirements, and incidence of side effects. There appears little justification for the use of the less familiar, and potentially more dangerous, thoracic approach when fentanyl alone is infused into the epidural space.

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Intra-ocular pressure changes using the laryngeal mask airway and tracheal tube

R. HOLDEN, C. D. G. MORSMAN, J. BUTLER, G. S. CLARK, D. S. HUGHES AND P. J. BACON

Summary

Intra-ocular pressure was measured before and throughout airway establishment with either the laryngeal mask airway or tracheal tube. Similar measurements were made on removal of either airway and the amount of coughing noted in the first minute after removal. There was a significantly smaller increase in intra-ocular pressure ($p < 0.001$) using the laryngeal mask airway, both on placement and removal, than with the tracheal tube. Postoperative coughing was significantly reduced using the laryngeal mask airway ($p < 0.001$). There was a significantly greater rise in heart rate using the tracheal tube ($p < 0.01$) probably related to an increased cardiovascular response. The laryngeal mask airway is recommended as an alternative to tracheal intubation in routine and emergency intra-ocular surgery.

Key words

Eye; intra-ocular pressure.
Equipment; laryngeal mask airway, tracheal tube.

The stress response to tracheal intubation and extubation is associated with a rise in intra-ocular pressure (IOP),[1–3] mainly due to increased ocular blood flow.[4] In perforating eye injuries a transient rise in IOP during intubation can be deleterious and increased IOP during extubation places a stress on wound closure, which is exacerbated by coughing. The Brain laryngeal mask airway is an alternative to the tracheal tube for artificial ventilation of the lungs in the paralysed patient.[5] The mask is placed directly over the posterior larynx, avoiding tracheal stimulation and so theoretically the systemic and ocular stress response associated with tracheal intubation and extubation is avoided. This prospective study compares the changes in IOP throughout tracheal intubation with that due to placement of the laryngeal mask airway. Intra-ocular pressure changes and coughing on removal of either airway were also compared.

Method

Ethics committee approval was obtained. Fifty-two patients scheduled to undergo elective general anaesthesia for cataract surgery were randomly allocated, by coin toss, into two groups of 26. All were ASA grade 1 or 2,[6] without a history of diabetes mellitus, hypertension, carotid artery disease or glaucoma. Patients were to receive intermittent positive pressure ventilation in one group using a laryngeal mask airway and in the other group using a tracheal tube. The anaesthetists in the study (J.B. and G.C.) regularly use both techniques in their normal practice. A standardised anaesthetic routine was used in all cases. Premedication with temazepam 10 mg, atropine 0.6 mg and ranitidine 150 mg orally was followed by induction with a sleep dose of etomidate 0.2–0.25 mg/kg and alfentanil 0.012 mg/kg. Neuromuscular blockade with vecuronium 0.1 mg/kg was monitored using a peripheral nerve stimulator. The patient's lungs were ventilated with 1.5% isoflurane in 100% oxygen for 3 minutes before intubation. At this point the anaesthetist was informed of the method for management of the airway.

The laryngeal mask airway was placed without using an introducer in one group of patients. In the other group, the larynx was sprayed with lignocaine 4% under direct vision and the trachea intubated using a RAE preformed tube. Anaesthesia was maintained with 66% nitrous oxide and 1.5% isoflurane in oxygen. The lungs were ventilated using a Penlon co-axial circuit and a Penlon Nuffield ventilator to maintain normal end-tidal carbon dioxide concentrations. Neuromuscular blockade was maintained with incremental doses of vecuronium, and reversed with neostigmine and

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Table 1. Baseline data for each group. Values are expressed as mean (SD).

	LMA	Tube	p
Sex ratio (M:F)	1:1	1:1.6	
Mean age; years	72.7 (12)	71.5 (10.6)	NS
Mean IOP before airway placement; mmHg	17.9 (3.8)	18 (4.1)	NS
Mean IOP before airway removal; mmHg	26.3 (5.9)	25.2 (5.4)	NS

IOP, Intra-ocular pressure; LMA, laryngeal mask airway; NS, not significant (Student's *t*-test).

glycopyrronium. The laryngeal mask airway or tracheal tube was removed once spontaneous ventilation was established.

A Clarke's lid speculum was used to expose the cornea of the non-operated eye which had previously been anaesthetised with benoxinate hydrochloride 4%. IOP was measured with the Alcon pneumotonometer which continuously records the IOP on a paper strip and digital meter. The accuracy of the pneumotonometer compares well with the Goldmàn tonometer.[7] Measurements were taken before and after induction, continuously during airway placement and thereafter for 30 seconds.

In all cases, the highest IOP was in the first 20 seconds of airway placement. The change in IOP was taken as the difference between postinduction IOP and the highest IOP recorded during airway establishment. The IOP was measured after reversal of neuromuscular blockade and then continuously during airway removal.

Coughing in the first minute after airway removal was classed as 'negligible' if there were less than five coughs or 'present' if there were more than five coughs. Cardiovascular parameters were recorded before and after induction of anaesthesia, and after airway establishment. The heart rate was continuously monitored and the blood pressure (BP) measured using a Dinamap 1846 automated sphygmomanometer set to record every 60 seconds during this period.

Cardiovascular parameters were not recorded at airway removal on the first 10 patients who formed a feasibility study.

Results

The sex ratio, mean age, and mean IOP before airway placement and airway removal in each group are shown in Table 1. The mean change in IOP during airway placement and removal is shown in Table 2. Tracings of typical pneumotonometer readings are shown in Figure 1. Ten patients in the tracheal tube group had negligible coughing in the first minute after extubation compared with 25 in the laryngeal mask airway group. This difference is statistically significant (Chi-squared test = 17.1, $p < 0.001$).

J.B. anaesthetised 33 of the 52 patients and G.C. 19. There was no statistical difference between the anaesthetists with regard to IOP changes during airway placement and removal (Student's *t*-test) or postoperative coughing (Chi-squared test) in either group. The maximum IOP recorded during tracheal intubation was 44 mmHg compared with 28 mmHg during laryngeal mask airway placement (normal IOP 10–20 mmHg). The maximum pressure during

Table 2. Ocular changes. Values are expressed as mean (SD).

	LMA	Tube	p	CI
Mean change IOP during airway placement; mmHg	+1.8 (2.1)	+6.8 (5.5)	< 0.001*	2–7
Mean change IOP during airway removal; mmHg	+1.4 (1.4)	+5.0 (5.8)	< 0.001*	0–4

LMA, laryngeal mask airway; IOP, Intra-ocular pressure; *Mann–Whitney *U*-test; CI, 95% confidence interval.

Table 3. Cardiovascular changes. Values are expressed as mean (SD).

Airway placement	LMA ($n = 26$)	Tube ($n = 26$)	p
Mean change heart rate; beats/minute	+3.1 (10.2)	+15.3 (14.3)	< 0.01*
Mean change systolic BP; mmHg	+2 (21.5)	+16 (34.4)	NS
Mean change diastolic BP; mmHg	+8.6 (6)	+7.8 (6)	NS
Airway removal	**LMA ($n = 22$)**	**Tube ($n = 20$)**	**p**
Mean change heart rate; beats/minute	+0.9 (7.6)	+3.9 (10.3)	NS
Mean change systolic BP; mmHg	−0.1 (12.4)	+7.7 (13.4)	NS
Mean change diastolic BP; mmHg	−0.5 (10.2)	+3.2 (10.8)	NS

LMA, laryngeal mask airway; NS, not significant (Student's *t*-test); *Student's *t*-test.

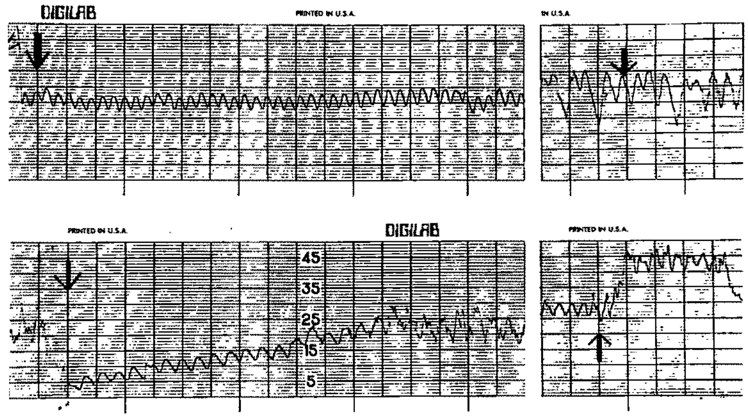

Fig. 1. Pneumotonometer tracing throughout placement of laryngeal mask airway (top left) and removal (top right), and throughout tracheal tube insertion (bottom left) and removal (bottom right). Arrow indicates start of each procedure. Intra-ocular pressure in mmHg. One abcissa square = one second.

removal of the tracheal tube was 48 mmHg compared with 33 mmHg using the laryngeal mask airway. One patient monitored whilst coughing had a peak IOP of 54 mmHg. The cardiovascular responses to placement and removal of the airway in each group are shown in Table 3.

Discussion

To our knowledge there are no studies in the literature in which the effect on IOP of placing a laryngeal mask airway is compared with that of tracheal intubation. In this study the change in IOP was significantly lower using the laryngeal mask airway. Previous studies of IOP changes during intubation have tended to take periodic measurements of the IOP, with a hand-held instrument, after a delay of about one minute.[1–3] This would miss the peak pressure, which we found to occur in the first 20 seconds. The mean changes in IOP during airway placement in either group are not clinically important. However, the maximum IOP recorded during tracheal intubation was greater than 40 mmHg in some patients and this may be important, particularly in penetrating injuries. The tracheal tube group had a significantly greater change in heart rate. These readings were taken continuously during airway placement therefore they indicate a greater cardiovascular response in this group. The BP readings were not instantaneous and although there was not a significant difference between the two groups with regard to the BP, the trend was for the systolic BP to be higher in the tracheal tube group. This lack of significance may have been due to the fact that the BP monitoring was not continuous. Further studies with instantaneous measurement of BP would be required to clarify this.

The standardisation of conditions for airway removal is more difficult than airway placement and at this stage the anaesthetist was aware of the type of airway. Both these factors have to be taken into account when the results of airway removal are interpreted. The change in IOP and amount of coughing was significantly lower in the laryngeal mask airway group. At this stage, coughing probably has a greater effect on the IOP than airway removal itself. The mechanism is likely to be similar to that of the Valsalva manoeuvre, in which raised intra-thoracic pressure is transmitted to the ocular veins thus raising the IOP.[8] Although only one patient's IOP was monitored whilst actually coughing, the IOP of greater than 50 mmHg probably reflects what usually occurs, therefore a reduction in coughing in the immediate postoperative period is evidently desirable.

The laryngeal mask airway caused a smaller rise in IOP than the tracheal tube, both on placement and removal. This is likely to be due to a decreased cardiovascular response. Furthermore, postoperative coughing is reduced with the laryngeal mask airway. These findings should be taken into account when considering the type of airway maintenance for anaesthesia in routine and emergency intra-ocular surgery.

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Protamine—the need to determine the dose

Comparison of a simple protamine titration method with an empirical dose regimen for reversal of heparinisation following cardiopulmonary bypass

J. F. KEELER, M. V. SHAH AND S. D. HANSBRO

Summary

A simple method of protamine titration using the Hemochron system was compared with an empirical dose protocol for reversal of heparinisation following cardiopulmonary bypass in 40 patients undergoing elective myocardial revascularisation. Protamine titration revealed a wide range for protamine requirement and resulted in a significant reduction in protamine dose compared with the empirical dose protocol ($p < 0.01$). Heparin reversal was assessed as adequate in all patients. The titration technique was easy and straightforward to use in the operating theatre.

Key words

Blood, coagulation; protamine, heparin.

Heparinisation is required for the safe performance of cardiopulmonary bypass, but at the end of the procedure, residual heparin needs to be reversed with protamine sulphate. Conventional protocols calculate the dose of protamine empirically, based on the patient's weight or the dose of heparin administered. There is considerable variation in the individual's response to heparin and protamine and this empirical approach cannot guarantee optimal heparin reversal.

Protamine has well documented side effects.[1] Hypotension is common but may be limited by adequate maintenance of the cardiac filling pressure. Cardiac output is usually well maintained if left ventricular function is good.[2] More serious reactions such as anaphylaxis or pulmonary vasoconstriction occur less frequently but may be catastrophic. Protamine causes thrombocytopaenia, may impair platelet aggregation, and exerts an anticoagulant effect due to an interaction with thrombin.[3] It is therefore undesirable to give more protamine than is necessary for heparin reversal.

Titration of the protamine requirement may allow more accurate dose calculation and thus avoid the problems of over- or underdosing. Recently, a simple titration method has been described using activated clotting time (ACT) measurement.[4] The use of sample tubes prefilled with fixed amounts of protamine allows the construction of a two-point dose-response line from which the required protamine dose can be calculated. However, this method has not been evaluated in a controlled clinical trial, nor with any laboratory tests, to assess the adequacy of heparin reversal. This study was designed to compare, in patients following cardiopulmonary bypass, the protamine dose determined from a similar, simple protamine titration slope with that calculated from an empirical method.

Method

Local ethics committee approval was obtained for this study. Informed consent was obtained from patients undergoing elective myocardial revascularisation operations. Patients presenting for reoperation, concomitant valve or left ventricular aneurysm surgery were excluded from the study, as were those who required the use of an intra-aortic counterpulsation device, a cell saver/haemoconcentrator or the administration of clotting factors during surgery. The anaesthetic technique was determined by the individual anaesthetist but the same type of cardiopulmonary bypass equipment was used in each case.

A baseline ACT was measured in all patients using the Hemochron apparatus. This system determines the time taken for a 2 ml blood sample to clot when placed in a tube containing 12 mg of diatomaceous earth. Heparinisation was then commenced with 300 IU/kg and additional heparin given as necessary during bypass to maintain the

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ACT at greater than 400 seconds. Patients were randomly allocated to receive, at the end of cardiopulmonary bypass, either an empirical protamine dose of 6 mg/kg, as routinely used in our hospital prior to the study (group 1), or a titrated protamine dose, calculated as described below (group 2). In group 1 the ACT was measured 10 minutes after protamine administration and if it had not returned to baseline levels, a further dose of protamine was given.

Protamine titration

Five to 10 minutes before the end of bypass, two simultaneous ACT determinations were performed: one sample was put in a standard protamine-free tube (status ACT) and the other in a tube containing a predetermined quantity of protamine in addition to the diatomaceous earth (P-ACT). If the ACT during bypass was 699 seconds or less, the second tube contained sufficient protamine to produce a final concentration of 0.015 mg/ml after the addition of the 2 ml blood sample. If the ACT was more than 700 seconds, the tube contained sufficient protamine to produce a final concentration of 0.020 mg/ml after the addition of a 2 ml blood sample.

These two ACT values were plotted against protamine concentration in the sample tubes and the line joining them extrapolated to cross the baseline ACT. This intercept, called the Unit Protamine Concentration (UPC), represents the amount of protamine required to neutralise the heparin in 1 ml of the patient's blood (see Fig. 1).

The protamine dose required was calculated by multiplying the UPC by the patient's blood volume, adjusted to take account of the volume of the extracorporeal circuit. The patient's blood volume was estimated from a height/weight nomogram with the volume of pump prime and cardioplegia solution added to produce an adjusted blood volume. The volume of blood remaining in the extracorporeal reservoir at the end of bypass was then subtracted from this value to give a final adjusted blood volume (ABV). Other fluid loss or administration was discounted as suggested by LaDuca and co-workers.[5]

Protamine indexing

Protamine preparations may vary in potency and it was necessary to determine the potency of the protamine used clinically relative to that contained within the assay tubes. This was carried out before the start of the study. A solution containing 1 mg/ml of the clinical protamine was prepared by dilution with 0.9% sodium chloride. Aliquots of this solution were added to two standard ACT tubes to produce concentrations of 0.015 mg/ml and 0.020 mg/ml protamine after the addition of a 2 ml blood sample. Heparin neutralisation curves were constructed for both protamine preparations using a heparinised blood sample obtained from one of the authors. The relative potency of the protamine was calculated by dividing UPC (clinical protamine) by UPC (assay protamine). This gave an index of 1.14 for our clinical protamine.

The final dose of protamine was calculated thus: Unit Protamine Concentration × Adjusted Blood Volume × Index.

Five minutes after the protamine had been given, verification of heparin reversal was performed in both groups by simultaneous ACT estimations in a standard tube and in one containing 0.005 mg/ml protamine. If status-ACT had not returned to the baseline value and if the p-ACT was closer to the baseline, a further neutralisation line was constructed as before, a dose calculation performed and additional protamine given.

Adequacy of heparin reversal was assessed in all patients by serial determinations of ACT and thrombin time (TT) at 5, 10 and 30 minutes after protamine administration and on admission to the intensive care unit. Blood was transfused postoperatively as determined by clinical parameters to maintain an adequate preload and a haematocrit around 0.30. The volume infused was recorded, as was the volume of blood lost postoperatively. Chest drains were removed on the day following surgery when drainage was less than 10 ml/hour for two consecutive hours.

Differences between the groups were compared using Student's *t* test for unpaired data except for sex distribution data where the chi-squared test was used. A value of $p < 0.05$ was considered significant.

Results

A total of 40 patients were studied. There was no significant difference between the groups with respect to age, sex distribution, weight or duration of cardiopulmonary bypass (Table 1). There was a wide variation in the protamine requirement in group 2 (Fig. 2) but these patients received significantly less protamine (mean 4.49 mg/kg, SD

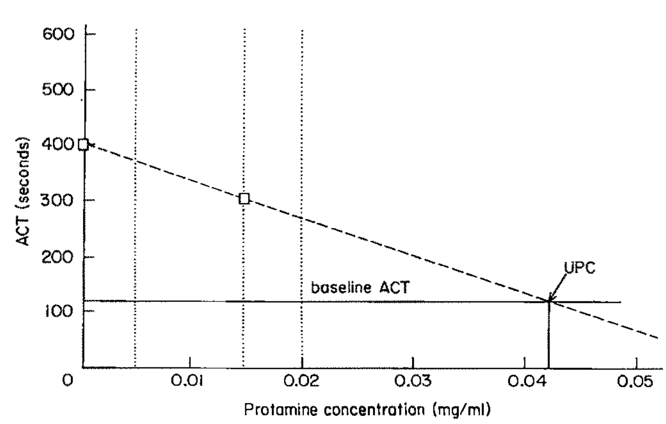

FIG. 1. Protamine titration slope example. □ = ACT values in the two tubes (399 and 302 seconds respectively); Unit Protamine Concentration (UPC) = 0.044 mg/ml; baseline ACT = 115 seconds.

Table 1. Descriptive data and duration of cardiopulmonary bypass (mean SD) except *simple ratio).

	Group 1	Group 2	p
Age; years	54.0 (8.14)	58.4 (7.18)	NS
Sex distribution; M/F*	18/2	15/5	NS
Weight; kg	74.7 (6.84)	75.0 (12.6)	NS
Time on bypass; minutes	94.4 (19.4)	87.3 (27.5)	NS

Table 2. Protamine dose, blood loss, blood administered and duration of chest drainage (mean (SD) (range)).

	Group 1	Group 2	p
Dose of protamine; mg/kg	6.2 (0.79) (5.3–9.3)	4.49 (1.64) (2.1–7.4)	< 0.01
Blood loss; ml			
(a) 0–3 hours post bypass	317 (209) (40–900)	272 (153) (82–630)	NS
(b) 0–24 hours post bypass	995 (492) (255–2000)	769 (286) (455–1270)	NS
Blood administered; ml	558 (422) (0–1400)	633 (477) (0–1250)	NS
Duration of chest drainage; hours	21 (4.1)	20.8 (6.3)	NS

1.64, range 2.1 to 7.4 mg/kg) than those in group 1 (mean 6.2 mg/kg, SD 0.79, range 5.3 to 9.3 mg/kg). Postoperative blood loss, volume of blood administered and the duration of chest drainage were similar in both groups (Table 2). Activated clotting and thrombin time values were expressed as ratios of the baseline ACT and the control thrombin time respectively. There was no significant difference between the groups with respect to these ratios (Figs 3 and 4).

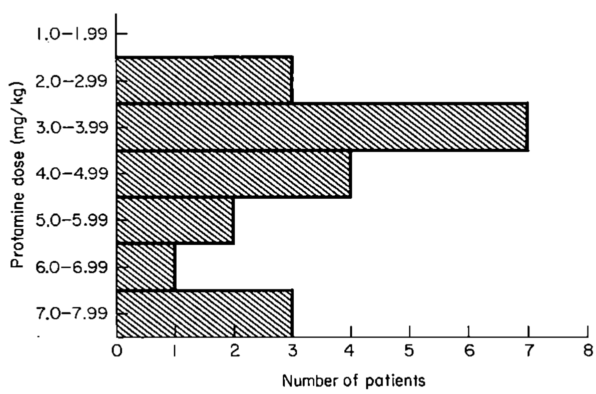

FIG. 2. Distribution of protamine doses in group 2.

Discussion

We have demonstrated a wide variation in the protamine requirement for heparin reversal following cardiopulmonary bypass (range 2.1 to 7.4 mg/kg body weight or 0.60 to 1.82 mg/100 IU heparin administered). This finding has been reported by other workers using a variety of titration methods.[4–6] This suggests that if the protamine dose is calculated empirically on a mg/kg, or indeed a mg/units heparin given, basis under- or overdosing is likely in a significant proportion of patients. Use of the dose response curve described by Bull[7] may help by individualising the heparin dose but the protamine dose is still given empirically; further, this does not take into account the variation in potency of different protamine preparations. Previously

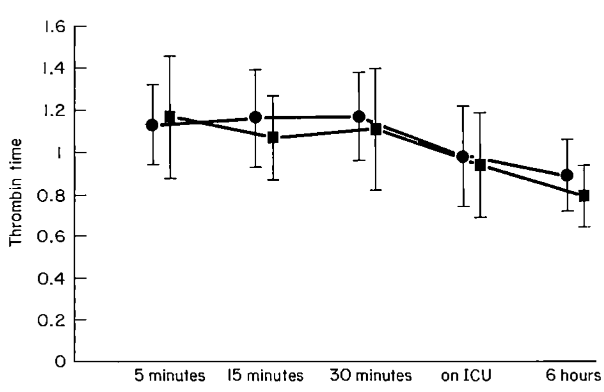

FIG. 3. Thrombin time (mean and SD) expressed as a ratio of control value at 5, 15 and 30 minutes after protamine administration, on admission to ICU and at 6 hours after protamine. ●, empirical dose (group 1), ■, titrated dose (group 2). (There was no significant difference between the groups.)

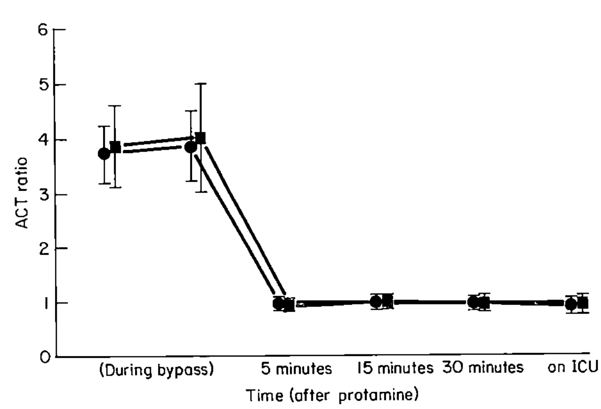

FIG. 4. ACT values (mean and SD) expressed as a ratio of baseline ACT, during cardiopulmonary bypass, at 5, 15 and 30 minutes after protamine administration, and on admission to ICU. ●, empirical dose (group 1); ■, titrated dose (group 2). (There was no significant difference between the groups.)

described methods of protamine titration have either required laboratory facilities or, if suitable for use in the operating theatre, have necessitated the construction of multiple point response curves using protamine solutions which is both time consuming and labour intensive.[4] Titration of the protamine dose, incorporating protamine indexing, as described earlier, has theoretical advantages.

Heparin reversal

The previous work using this technique has shown adequate reversal of heparinisation but has not attempted a direct comparison with a group receiving an empirical protamine dose, the comparison being with historical controls.[5,6] Nobody has previously assessed the adequacy of heparin reversal produced by this method of titration using laboratory tests of the coagulation system, reliance being placed on the ACT estimation. ACT is widely used for monitoring heparinisation during cardiopulmonary bypass because it is readily available, cheap, easy to use in the operating theatre and provides rapid results. However, accuracy may be impaired by a number of factors including excessive haemodilution, hypothermia and high heparin levels. It has recently been criticised by Hooper *et al.*[8] as an insensitive indicator of residual heparinisation. Standard laboratory tests of coagulation are inappropriate for use during cardiopulmonary bypass because they are too sensitive and logistically difficult to organise. However, they are useful for the assessment of residual heparinisation following protamine administration. Penner[9] suggested that the thrombin time was the most appropriate test for monitoring heparin therapy. Our study demonstrates adequate heparin reversal with both the titrated and the empirical protamine dose as assessed both by serial ACT and thrombin time estimations. Thrombin time in our study returned to, and remained at, control levels in both groups following protamine administration, suggesting minimal residual heparin. Postoperative blood loss was not significantly different between the two groups. There was no evidence of heparin rebound.

A dose of 6 mg/kg protamine might be considered high by some clinicians but two patients in the empirical group required additional protamine as judged clinically and with the Hemochron (7.3 and 9.3 mg/kg). Four patients in the titrated group also required greater than 6 mg/kg protamine. Even if a lower empirical dose had been chosen it would not have been appropriate for every patient. The titration method was able to predict the variation in protamine requirement in individual cases. This resulted in the average dose in the titrated group being significantly less than that in the empirical group in our study. Rivard and Thompson studied 317 patients and found the titrated dose to be less than that obtained from a Bull dose/response curve in 95% of cases.[6] Thus the dose estimated by titration is generally less than that calculated empirically. However, it is not acceptable just to reduce the empirical dose by a set proportion because of the variability in protamine requirement; protamine dose varied three-fold in our study. Titration of the dose offers a method to match each patient's dose to his or her need.

In summary, the protamine requirement for heparin reversal following cardiopulmonary bypass showed wide individual variation. Calculation of the protamine dose by titration resulted in a reduction in protamine dose in the majority of cases without any deleterious effect on heparin reversal. The method described was simple and easy to use in the operating theatre. No patient had a significant reaction to protamine administration.

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Acute tolerance from benzodiazepine night sedation

T. G. SHORT AND D. C. GALLETLY

Summary

The hypothesis that benzodiazepine night sedation causes acute tolerance to benzodiazepine sedation given the following morning was examined in six volunteers in a double blind, randomised, crossover study. Before each of three study days, subjects received midazolam 15 mg or flunitrazepam 2 mg or placebo as oral night sedation. They were then given intravenous midazolam 5 mg the following morning and the resulting sedative effects examined, using an observers sedation scale and a psychomotor test battery (critical flicker fusion frequency, digit-symbol substitution, reflex time, tapping test and a visual analogue sedation scale). Although a consistent pattern emerged with the greatest degree of sedation following the placebo night sedation and the least degree of sedation following the midazolam, with flunitrazepam intermediate, no statistically significant differences were present between the three treatment groups. The results indicate that single use of benzodiazepine night sedation is not an important influence on benzodiazepine requirements for intravenous sedation.

Key words

Hypnotics benzodiazepine; midazolam, flunitrazepam.
Acute tolerance.

It is widely recognised that individuals differ markedly (up to 22-fold) in the dose of benzodiazepine required for satisfactory intravenous sedation.[1] An important cause of increased benzodiazepine dose requirement is tolerance occurring in patients who chronically ingest oral benzodiazepines. Such patients may need more than twice the dose required by naive patients, to produce the same sedative effect.[1] Tolerance following a single dose has also been demonstrated in laboratory animals.[2,3] In patients undergoing important surgical procedures, benzodiazepines are commonly administered on the evening before surgery and it is possible that in part, the wide interindividual variability in response to intravenous benzodiazepines for sedation is because of acute tolerance following night sedation. To test this hypothesis we examined the psychomotor effects of intravenous midazolam the morning following either midazolam, flunitrazepam or placebo night sedation in human volunteers.

Methods

The study was performed on six volunteers, three male and three female, mean age 27 (range 22–35) years, weight 72 (range 57–86) kg and height 178 (range 160–195) cm. All were healthy, were taking no psychotropic medication and had refrained from alcohol and caffeine-containing beverages for the 24 hours before each study period. Local ethics committee approval was obtained before starting the study and informed consent was obtained from each volunteer.

The study was performed according to a double blind, random order, Latin square, crossover design with three study periods. Each study period was separated by a time interval of 2 weeks. All data were recorded by the same investigator. Before the study, all subjects were familiarised with a psychomotor test battery to reduce learning effects. The psychomotor/sedation test battery consisted of: (1) Critical flicker fusion frequency (taken as the average of six readings); (2) Digit-symbol substitution (time to complete 16 substitutions); (3) Simple reflex time (mean value of 30 attempts); (4) Tapping test (number of times button pressed in 30 seconds); (5) A linear analogue sedation scale (10 cm line with extremes denoted 'alert' and 'drowsy').

Each of the three study periods lasted 2 days. At 08.30 hours on day one, volunteers completed the psychomotor/sedation test battery. That evening, subjects retired between 22.00 and 23.00 hours after ingesting one of the following oral compounds, administered in coded gelatine capsules; (a) midazolam 15 mg, (b) flunitrazepam 2 mg, (c) placebo (dextrose).

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Table 1. Sedation scale.

0	No observable sedative effects
1.	Minimal sedative effects
2.	Drowsy, partial lid closure
3.	Upper lid bisects pupil or full lid closure, responding to verbal command
4.	Unresponsive to verbal command, responds to mild physical stimulus (tapping shoulder)
5.	Responsive to painful stimulus (trapezius squeeze)
6.	Unresponsive

At 08.30 hours the following morning, the volunteers repeated the psychomotor/sedation test battery. They then received intravenous midazolam 5 mg over 10 seconds via a 20 gauge cannula inserted in the non-dominant forearm. For the next 10 minutes they were asked to keep their eyes open at 30 second intervals, and before each instruction the degree of sedation observed was recorded according to a seven point sedation scale (Table 1). Heart rate, non-invasive blood pressure ('Dinamap'), respiratory rate and end-tidal carbon dioxide (nasal cannulae with 'Datex' CO_2 analyser) were recorded at one minute intervals for 10 minutes. The psychomotor/sedation and motor coordination test battery was then repeated 15 minutes after midazolam administration. The study plan is summarised in Table 2.

Statistical analysis

The psychomotor tests and visual analogue mood scales were treated as parametric data. Analysis of variance was used to compare the baseline tests on day 1 with the baseline tests on day 2 (the residual sedation effect) and the baseline test on day 1 against that immediately following the intravenous midazolam (the acute tolerance effect). Sedation scores during the 10 minute period following midazolam injection were compared by summing sedation scores for the 10 minute period and comparing the three drug groups using Kruskal-Wallis nonparametric analysis of variance.

Table 2. Study plan.

Day 1	
08.30 hours	Psychomotor/sedation test battery
22.00–23.00 hours	Oral midazolam 15 mg, flunitrazepam 2 mg or placebo
Day 2	
08.30 hours	Psychomotor/sedation test battery
09.00 hours	Intravenous midazolam 5 mg
09.00–9.10 hours	Clinical and physiological evaluation of sedation
09.15 hours	Psychomotor/sedation test battery

Results

Residual sedation

The linear analogue sedation scale showed a significant difference ($p < 0.05$) between drug groups, subjects being more drowsy if they had received an oral benzodiazepine; the decreasing order of residual subjective drowsiness was flunitrazepam (19 mm), midazolam (10 mm) and placebo (3 mm). None of the results of the psychomotor tests changed significantly from the pretreatment values.

Acute tolerance effect

The linear analogue sedation and psychomotor effects 15 minutes following the intravenous midazolam are summarized in Table 3. All measures showed the expected deterioration in performance following midazolam injection. However, there was no significant difference in the degree of impairment produced between the three groups with any of these tests or with the physiological monitoring. It was of note, however, that both the observer's sedation scale, and all but one of the psychomotor battery of tests showed a consistent pattern; the greatest sedation occurred after placebo night sedation and the least sedation occurred after midazolam night sedation. Flunitrazepam was intermediate.

Discussion

Acute tolerance to benzodiazepines is a well described phenomena. After an oral dose of diazepam 0.07 mg/kg given to human subjects, psychomotor effects that were demonstrable during the initial rise in plasma concentration had disappeared by the time the concentration had returned to the same level during the recovery phase.[4] A similar effect is also seen during recovery from intentional benzodiazepine overdoses.[5] In laboratory animal studies, markedly diminished psychomotor effects are observed when a dose of benzodiazepine is repeated after an interval of 24 hours. Mice given intraperitoneal diazepam 30 mg/kg 24 hours previously, had a mean duration of sleep following diazepam 35 mg/kg of 5 minutes, compared to 45 minutes in controls who had no prior exposure to diazepam.[2] After diazepam 5 mg/kg by mouth, the inability to run on a rotarod test was reduced from 58 minutes after the first dose to 25 minutes after a second dose 24 hours later.[3] Although the mechanism of acute tolerance is

Table 3. Change in observer's sedation score and psychomotor tests following intravenous midazolam 5 mg (mean SEM). The change is from the pretreatment score (day one for the psychomotor tests). There were no statistically significant differences between the three treatments.

	Midazolam	Flunitrazepam	Placebo
Sedation score; mean over 10 minutes	+2.6 (0.2)	+2.6 (0.1)	+2.7 (0.1)
LAS alert/drowsy; change in mm	+24 (5)	+28 (3)	+32 (5)
Critical flicker fusion frequency; Hz	−6.4 (1.0)	−6.6 (0.7)	−7.6 (0.9)
Digit-symbol substitution; seconds	+45 (10)	+40 (9)	+48 (12)
Simple reflex time; seconds	+1.7 (0.1)	+1.7 (0.1)	+1.9 (0.1)
Tapping test; number of taps	−73 (12)	−68 (9)	−72 (13)

unknown it has been demonstrated that neither acute nor chronic tolerance is due to pharmacokinetic changes.[2,4,6]

In this present study we administered benzodiazepines to human volunteers in a manner that reflects hospital practice; standard doses of midazolam or flunitrazepam as night sedation, followed the next day by a standard intravenous sedative dose of midazolam, as may be used for a therapeutic procedure. We were unable to detect acute tolerance when using them in this way, although a pattern consistent with acute tolerance occurred, with the greatest sedation seen when placebo had been given the night before; the least sedation occurred when midazolam had been given and flunitrazepam caused intermediate effects.

We chose midazolam (with an elimination half-life of 1.5–2 hours) and flunitrazepam (with elimination half-life of 14–16 hours) in order to compare a short acting benzodiazepine that is essentially eliminated from the body before the second dose is given 10 hours later, with a long acting benzodiazepine that will still have significant blood levels at the time of second dose. Our inability to detect significant acute tolerance is unlikely to influence our choice of these agents since both midazolam (in rats)[7] and flunitrazepam (in humans)[8] have been demonstrated to cause tolerance. It is also unlikely that the choice of a 10 hour time interval between doses affected the development of tolerance, as this time lies between the acute tolerance demonstrated after single doses that occurs within 4 hours[2] and acute tolerance demonstrated in studies on mice maximal at 24 hours after the initial dose.[4–6] Our failure to observe acute tolerance is likely to be because we use clinical doses rather than the higher doses used in laboratory studies.

We saw no acute tolerance when a standard midazolam or flunitrazepam oral night sedation was followed by standard intravenous midazolam sedation the following morning. However, a trend consistent with acute tolerance was seen, with the greatest sedation occurring after placebo and the least sedation following midazolam night sedation. We conclude that acute tolerance from night sedation and residual effects after a single dose of flunitrazepam do not contribute significantly to the large variability in effect seen with standard intravenous doses of benzodiazepine for sedation.

Acknowledgment

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CASE REPORT

Hysteria

A cause of failure to recover after anaesthesia

A. P. ADAMS AND T. GOROSZENIUK

Summary

Hysteria as a cause of failure to recover consciousness following general anaesthesia is a rare event. This case report describes such an instance in a young, healthy 22-year-old female suffering severe dental phobia who was undergoing dental conservation. The literature is reviewed and a summary of the possible physiological mechanisms involved is given.

Key words

Complications; hysterical anaesthesia.
Recovery; prolonged.

Cases of hysterical anaesthesia in conscious patients are not common and most have been studied in the psychiatric setting.[1] Hysteria as a cause of failure to regain consciousness after general anaesthesia is a very rare occurrence. We report such a case in a young, physically healthy female.

Case history

A 22-year-old female patient, who weighed 64 kg and who had once studied as a nurse, presented for dental treatment as an outpatient. She had a severe dental phobia of 13 years' duration and would only contemplate dental treatment on condition that she could receive a general anaesthetic. During a stay in Germany 5 years previously the patient had received some kind of desensitisation treatment for her dental phobia, the details of which were unavailable.

There was no relevant medical or family history, except that 3 years previously, the patient 'passed out' during a visit to the hospital dentist and was admitted to a ward: she was hypotonic, unresponsive to verbal command and to painful stimuli and remained in this condition for the next 11 days. Neurological and general physical examination and electroencephalography (EEG) were entirely normal. During this time the only treatment consisted of intravenous fluids. On the 12th day after admission, the patient's level of consciousness improved dramatically and over the next 18 days she underwent psychiatric examination, during which time she became agitated and distressed. The extracts from her notes describe her as 'an extremely immature young woman' and her condition as 'hysterical stupor' with further comments '... suggestive of underlying conflict or complication, the nature of which remains unclear'. Follow-up psychiatric observations could not be made because the patient failed to keep appointments.

The patient, who was receiving no current medication, had been well prepared by the dental surgeons and since she was surprisingly cooperative no premedication was given. General anaesthesia was induced with alfentanil 5 μg/kg, methohexitone 1.5 mg/kg and vecuronium 0.1 mg/kg followed by nasotracheal intubation with a cuffed 6.0 mm RAE pattern Mallinckrodt tube. The surgery, which consisted of extensive conservation work on the teeth, lasted for 75 minutes. Anaesthesia was maintained with nitrous oxide in 33% oxygen with 0.75% isoflurane, and intermittent boluses of alfentanil and vecuronium to total doses of 700 μg and 7 mg respectively. Intermittent positive pressure ventilation of the lungs was maintained using a Bain-type anaesthetic breathing system and Penlon Nuffield 200 series ventilator; fresh gas flow was adjusted to 70 ml/kg/minute to maintain normocarbia and $F_{E'}CO_2$ was continuously monitored using a Datex Cardiocap monitor. Intra-operative monitoring included continuous display of the CM5 lead of the electrocardiogram (ECG), heart rate, and haemoglobin oxygen satura-

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tion (finger probe), and automated recording of noninvasive blood pressure every 3 minutes. The degree of neuromuscular blockade was assessed intermittently using a peripheral nerve stimulator.

All vital signs were stable throughout surgery and anaesthesia: arterial pressure remained stable at 125/70 ($\pm$5) mmHg, heart rate was 115 beats/minute before induction and 74 beats/minute at the end of operation; the train-of-four response to neuromuscular stimulation of the ulnar nerve at the wrist was maintained at 30–40%. At the end of the procedure spontaneous ventilation returned (train-of-four, 75–80%) without the need for antagonism of the residual effects of the vecuronium. The tracheal tube was removed and the patient transferred to the adjoining recovery room. During the recovery period her cardiovascular and respiratory systems remained stable. However, the patient remained unconscious; her pupils were equal and reacted normally to light. Reflexes were normal, but she did not respond to verbal commands nor to the application of painful stimuli to the limbs or chest. Administration of naloxone 0.4 mg, followed 10 minutes later by doxapram 100 mg, failed to affect the level of consciousness. The patient was then stimulated by a short period of rebreathing, again without success. Passage of a soft suction catheter through the nose produced virtually no effect other than a slight stimulation of the depth of breathing and some tremor of the eyelids. A full physical examination of the patient was entirely normal. Four hours after the end of the anaesthetic a tetanic stimulus (50 Hz for 5 seconds) was applied to the ulnar nerve at the wrist using the peripheral nerve stimulator; the response was dramatic. She opened her eyes and sat up on the bed, fully orientated in space and time, and announced she was sorry and was now ready to go home. The patient was accompanied home by her parents who were fortunately very grateful for the care extended to their daughter.

Discussion

The reason that 9.3 million people in the UK avoid dentists is sheer funk, or dental phobia, which has been described as 'the holy trinity of fear, pain and the dentist'.[2] The 10-year survey of adult dental health in the UK showed that, up to 1978, only 43% of 5697 patients interviewed went to a dentist for check-ups on a regular basis; 14% of patients went occasionally, and 43% would attend only if they had pain.[3] Although there were many reasons given by those who did not attend regularly, 26% of these patients gave their reason as being 'scared'. Patients' attitudes and behaviour are also reflected when geographical factors are considered: of those patients regularly attending for check-ups, only 35% came from the North-West, compared with 50% from the South-West, of England. These two areas represent the 'worst' and the 'best' parts of the country as far as dental attendance is concerned. The latest report,[4] covering the 10 years to 1988, showed an improvement (to 50%) in the numbers of dentate adults attending for regular check-ups; 36% sought treatment because they were 'in trouble' and 14% occasionally attended for a check-up. In a sample of 3527 dentate adults, the main barriers to dental care were found to be fear (45%), the perceived image of the dentist or surgery (22%), or the cost (22%), whereas the remaining 11% of patients interviewed perceived no strong association with any of these factors.[4]

The terms hysteria and hysterical are widely used in many branches of medicine and hysteria is one of the few psychiatric diagnoses which nonpsychiatrists commonly make with any confidence.[5] However, there is a real possibility that the diagnosis may eventually turn out to be an organic one.

The charactistics of hysteria include immaturity, histrionic behaviour, sexualization of relationships, low frustration tolerance, shallow interpersonal ties, and dependency. Hysterical neurosis may be of the conversion type, with physical symptoms involving voluntary musclature and the sensory system, such as paradoxical paralyses, seizures, sensory deficits and pain, and there is an attitude of indifference. The dissociative type of hysteria is associated with alterations in consciousness and sense of identity, such as fugue states, amnesias, and somnambulism, but anxiety is not evident.[6]

Failure to recover consciousness following a general anaesthetic usually has some obvious cause related to the types of drug and dosage used, in the context of the patient's overall size and fitness; there is always the fear of a period of unrecognised severe hypoxia causing brain damage. Uncommon causes include a cerebrovascular accident, hypothermia, or some previously unrecognised endocrinological disorder, such as hypothyroidism.

Assessment was directed to a thorough and repeated examination of the patient to ascertain whether there was an organic cause. It is particularly important to exclude epilepsy and schizophrenia.[5–7] All drugs and used ampoules were carefully checked, in case an error had been made. The diagnosis of hysteria was made on exclusion of other possibilities and from the presence of certain signs. These included an intermittent flickering of the eyelashes, and the fact that, when the patient's arm was raised and let fall, she always prevented it from hitting her face. It was surprising that the usual arousal or painful tests which were applied, as are commonly used in the neurological or neurosurgical assessment of patients in coma (sternal pain, pressure to digits), failed to arouse her. The response to electrical stimulation of a peripheral nerve proved to be irresistible and dramatic. This may not be surprising, since a supramaximal stimulus of 55 mA is delivered by the nerve stimulator. Whether or not this stimulus would have been equally effective had it been applied much earlier is, of course, unknown.

There is little about hysteria in the anaesthetic literature. The subject was discussed in a paper from Japan in the context of general anaesthesia for oral surgery in patients suffering from hysteria, epilepsy and schizophrenia.[7] The most recent case of hysteria, concerning a 31-year-old female who worked in the psychiatric department of a Paris hospital, was reported in 1980 by Bouchard and his colleagues.[8] His patient also presented for dental treatment. Previous cases of failure to recover consciousness following general anaesthesia which were ascribed to hysteria include one of coma lasting several hours following a partial thyroidectomy for hyperthyroidism, another involving the inability of a patient to breathe after urological surgery with the diagnosis of hysteria provided by the patient's husband, and the third following a bronchoscopy in a young girl.[8] All the patients were women.

The cortical somatosensory averaged evoked response (AER) has been widely used to attempt to differentiate hysterical from organic disturbances and it is now generally

agreed that in hysterical subjects an AER can be recorded at a time when the subject fails to perceive the stimulus.[1] This approach has been used to distinguish cases of conscious patients presenting with hysterical anaesthesia, provided that care is taken to define the stimulus intensity and the site of application of the electrodes. Besides being of diagnostic value, this method may reveal important information about the neurophysiological mechanisms which mediate these hysterical disturbances. Skin stimulation at near threshold stimuli was used by Hernández-Peón and his colleagues,[9] whereas other workers[10–12] used nerve stimulation, although there is doubt about the stimulus intensity. The two approaches, skin versus nerve stimulation, produce conflicting results. It is suggested that when the stimulus is applied to a peripheral nerve the amplitude of the contralateral AER from the affected side is smaller at low levels of stimulation, but when the sensory stimulus is increased the two sides become equal. However, if peripheral receptors rather than nerves are being stimulated, the anaesthetic side produces a consistently smaller response irrespective of intensity, at least within the ranges used in these studies. It is suggested that there might be at least two different physiological mechanisms underlying hysterical anaesthesia:[13] a depression in peripheral receptor sensitivity, and a more central factor, possibly of the kind postulated by Hernández-Peón.[14]

Hysteria is a type of psychiatric illness and usually is confined to young females who are in the presence of other people. Typically, there is a contrast between a stable cardiovascular and respiratory state in the presence of flaccidity of skeletal muscles and coma. Testing to painful stimuli such as pinprick is associated with an apparent total loss of sensation. In Bouchard's case the patient, although seemingly unconscious, also always prevented the lifted arm from falling and injuring her face and a hysteric seldom hurts her own body. The past medical history is important in determining the diagnosis. However, as in so many other areas of medicine, such a diagnosis can only be entertained after detailed consideration of common and uncommon underlying diagnoses, coupled with the most rigorous and repeated assessment and examination of the patient.

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Note added in proof

Since the above case report was accepted for publication this patient has again presented to the same dental surgeon for further conservative dental surgery. Again, general anaesthesia was requested because the patient would under no circumstances permit the surgeon to work within the mouth. One of the authors (A.P.A.) administered the same anaesthetic drugs (in the same dosage) with the same anaesthetic technique as previously; the duration of surgery coincidentally was again 75 minutes. The patient made a normal recovery aided by use of the nerve stimulator at the end of anaesthesia. The patient's parents thought that their daughter's attitude to hospitals was improving since the previous anaesthetic and it can only be hoped that further general anaesthesia for conservative dental work may be avoided in the future.

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CASE REPORT

Double-blind testing fails to confirm analgesic response to extradural morphine

A. R. JADAD, M. T. POPAT, C. J. GLYNN AND H. J. McQUAY

Summary

We report two patients with chronic non-malignant pain in whom morphine given intravenously via a patient-controlled analgesia system produced partial pain relief but was accompanied by severe side effects. Open administration of epidural morphine resulted in complete pain relief with minimal side effects and the patients were considered as candidates for implanted opioid delivery systems. However, when the epidural morphine was given in a double-blind and placebo-controlled manner, morphine did not produce greater analgesia than placebo and no dose-response relationship was seen. These cases show that careful investigation is necessary before proceeding to implanted systems and that changing the route did not improve the analgesia : side effect balance for morphine in these patients.

Key words

Analgesics; morphine.
Anaesthetic techniques, regional; epidural.
Pain; placebo effect.

Spinal opioids, placed either intrathecally or extradurally, may, in some chronic pain patients, produce better analgesia with fewer side effects than oral or intravenous doses. Long-term delivery requires the implantation of an intrathecal or extradural catheter, with or without an internal pump. The potential morbidity and the cost of such implantation is considerable and it is necessary to be certain that there is potential benefit before embarking on the procedure.

We present two patients in whom open doses of extradural morphine produced complete pain relief after intravenous morphine via a patient-controlled analgesia system (PCA) had failed. Implanted systems for extradural opioid delivery were being considered but to confirm this beneficial response extradural morphine was given in a double-blind, placebo-controlled fashion.

Case histories

Both patients received intravenous morphine given via an Oxford PCA system (PRODAC),[1] with an incremental dose size of 0.5 mg and no lockout period. No loading dose or background infusion were given. Extradural drugs were given via a catheter inserted at the $L_{2\text{-}3}$ interspace under aseptic conditions. Catheter position was confirmed with local anaesthetic. Morphine 2, 5 and 10 mg diluted with normal saline to 10 ml and normal saline 10 ml (placebo), were administered extradurally, double-blind and in randomised order at 24-h intervals if the pain intensity was severe.

Pain measurement was performed with the McGill pain questionnaire, before and 24 h after starting PCA, a visual analogue scale (VAS) and a categorical scale for pain intensity (CSPI) before and during PCA and before and 3 h after each extradural injection. The VAS was a 100 mm straight line with 'least possible pain' at one end and 'worst possible pain' at the other. The patients were asked to put a mark on this line to reflect the current intensity of their pain.[2] The CSPI comprised four words: none, mild, moderate and severe. All the assessments were made by the same investigator. Volunteered current side effects were recorded by the same investigator using a four-point categorical scale (CSSE): none, mild, moderate and severe.

Patient 1

A 43-year-old woman with a 9-year history of multiple sclerosis was admitted to the Pain Relief Unit because she had been suffering from stabbing pains in her legs and in the left loin for the past 18 months. These pains were

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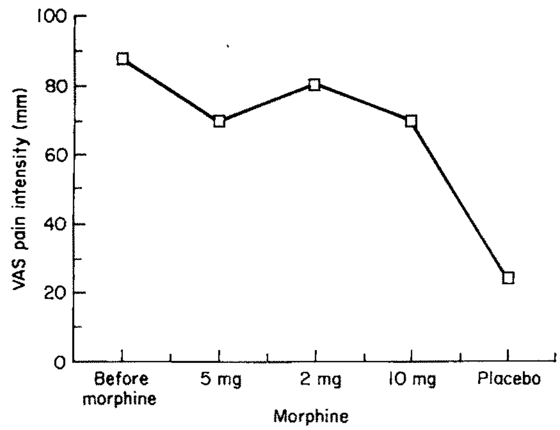

Fig. 1. Pain intensity before and 3 hours after extradural morphine and placebo in patient 1.

constant and worse when standing up. On examination, she was thinly built with an unstable gait. Muscle power and tone were normal and there was patchy loss of sensation to light touch and pinprick in the left leg. Vibration sense was absent distal to the left wrist and below the knees. Reflexes were brisk and symmetrical and the plantar responses were equivocal. She had been treated for the pain with various drugs including paracetamol, co-proxamol, ibuprofen and diclofenac without significant benefit. She had also practised relaxation techniques and hypnosis without improvement. Her current oral medication included baclofen 10 mg, carbamazepine 200 mg, diazepam 2.5 mg all four times a day, and gamolenic acid 120 mg, minocycline 50 mg and prednisolone 15 mg twice a day. On the McGill pain questionnaire she chose 25 words with a total score of 50. Her pain intensity was 91 on the VAS and severe on CSPI.

Intravenous morphine via PCA (38.5 mg over 24 h) produced partial relief of pain (CSPI moderate, a McGill score of 40 and 14 words chosen, and a VAS pain intensity of 75 mm) but also severe side effects, including nausea, drowsiness and giddiness. An extradural catheter was inserted and plain bupivacaine 0.5% 10 ml with methylprednisolone 80 mg was given with complete pain relief but only for the duration of numbness. Subsequently, the patient had extradural clonidine 150 μg, midazolam 5 mg and ketamine 10 mg at 24 h intervals with no pain relief. Forty-eight hours later, extradural morphine 5 mg produced complete pain relief, starting 90 min after the injection and lasting 72 h without any side effects. Over the next 5 days she had further extradural injections of morphine 5, 10 and 5 mg with complete pain relief, lasting 24, 22 and 6 h respectively. She was then discharged home on slow-release oral morphine (MST continus, Napp Laboratories) 20 mg twice daily with oral morphine solution (MSS) 20 mg as escape medication. This was subsequently increased to MST 40 mg twice daily with MSS 40 mg without any pain relief. The patient refused to increase the dose further for fear of side effects, regardless of reassurance.

She was readmitted and an extradural catheter was placed at the same level as before and injection of the same dose of bupivacaine produced complete pain relief with numbness. As complete analgesia without side effects had previously been obtained with extradural morphine, the patient was considered suitable for a long-term delivery system. Before embarking on this, we decided to confirm the opioid sensitivity of the pain using extradural morphine in a double-blind, placebo-controlled fashion. As shown in Figure 1, VAS pain intensity was 70 after morphine 5 mg, 80 after 2 mg, 70 after 10 mg and 24 after placebo. There were no side effects.

Patient 2

A 46-year-old woman was admitted to the Pain Relief Unit because she had been suffering from constant low back pain, radiating as a burning sensation to the legs for the last 4 years. Previous history included surgery for a prolapsed intervertebral disc in 1974 when a myelogram was performed using lophendylate (Myodil, Glaxo Laboratories Limited). This was followed by a pain-free period of 12 years. A repeat myelogram to investigate her present pain showed intrathecal adhesions and nerve roots matted with Myodil globules, suggesting arachnoiditis. On examination, she was tender over the T_{12}–L_5 spinous processes with practically no trunk movements due to pain. Straight-leg raising was 0 degrees on the left and 10 degrees on the right. Total sensory loss was demonstrated in the left S_1 dermatome. Right knee and both ankle reflexes were absent. Previous oral drug therapy included ibuprofen, amitriptyline, sodium valproate, temazepam, meptazinol and buprenorphine. Previously MST 30 mg twice daily had resulted in nausea and vomiting without pain relief. Her current oral medication included dihydrocodeine 30 mg four times a day, clonazepam 1.5 mg, prothiaden 150 mg and diazepam 10 mg daily. She had also had bilateral sympathectomy and intrathecal hyalase without any benefit. Extradural injections of local anaesthetic and steroids initally gave her 3 months relief but further injections failed to have an effect. Extradural phenol produced pain relief for 8 weeks and extradural clonidine had no effect. Pain assessments showed CSPI as severe, a McGill score of 57 and 18 words chosen, and a VAS pain intensity score of 95.

She obtained slight pain relief from the dihydrocodeine without side effects, so it was decided to use PCA morphine to test the opioid sensitivity of her pain. She was instructed to stop dihydrocodeine one week before admission. She received morphine 75.2 mg over 10 h via the PCA system, but this was stopped because of severe drowsiness, sweating, itching and lack of concentration. At that point, the CSPI was moderate and the VAS pain intensity score for her back pain was 47 and for her leg pain was 32. She felt that this was 'better than anything else before' but found the side effects unacceptable.

Forty-eight h after stopping PCA, plain bupivacaine 0.5% 6 ml with methylprednisolone 80 mg was given extradurally with complete pain relief, but only for the duration of numbness. Subsequently, she had clonidine 150 μg and ketamine 10 mg at 24-h intervals without any pain relief. Twenty-four h after the last injection, morphine 5 mg was given extradurally with complete relief of pain, which started after 60 min and lasted 15 h with only mild itching in the legs. Another dose of morphine 5 mg was given and the patient had complete pain relief, which lasted for 12 h without side effects.

As with patient 1, she was considered suitable for a long-term delivery system of extradural morphine. Therefore, we decided to confirm the opioid sensitivity of the pain by this

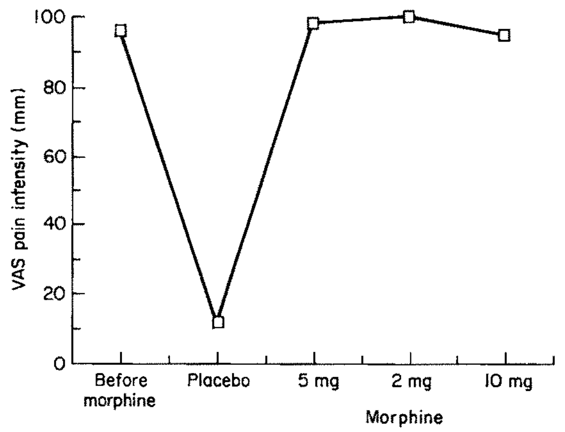

Fig. 2. Pain intensity before and 3 hours after extradural morphine and placebo in patient 2.

route by using morphine in the same double-blind, placebo-controlled fashion. In this case, VAS pain intensity was 12 after placebo, 98 after morphine 5 mg, 95 after 10 mg and 100 after 2 mg (Fig. 2). The only side effect reported was mild itching in the legs after morphine 5 mg.

Discussion

In both of these cases intravenous morphine produced partial pain relief with unacceptable side effects. In both patients open extradural doses of ketamine and clonidine (and midazolam in patient 1) failed to produce pain relief, but open doses of morphine given extradurally produced complete analgesia without significant side effects. Because of this, both patients were initially considered as candidates for implanted opioid delivery systems. However, when the extradural morphine was given in a double-blind, placebo-controlled fashion there was no significant pain relief. Our conclusion is that the relief seen with the previous open extradural doses was a placebo phenomenon. The moral for us is that we must prove the potential benefit of spinal opioids before implantation, and open trials are not adequate for this task.

We would defend the use of opioids, by whatever route, in the management of some patients with chronic non-malignant pain. As in these two cases, our criterion is that when nonopioid analgesics have been tried and failed and appropriate injection techniques have been tried and failed, opioids may be appropriate, but only if they provide effective relief. Given that the opioids produce effective relief, a secondary issue is then the best route of administration. If conventional routes produce only partial pain relief with a high side effect penalty, spinal routes are an alternative to obtain better analgesia with fewer side effects.[3,4] The rationale for this approach is unclear because, given by either conventional or spinal routes, opioids should reach the same receptors to produce both analgesia and side effects.[5]

These two cases illustrate the necessity of double-blind testing. Patients desperate for help may be so grateful, or simply polite, that measuring pain relief after open administration of analgesics is not a good enough basis on which to proceed to yet more invasive therapy. We would recommend therefore that testing for the effect of extradural opioids should be done double-blind with appropriate controls. A false-positive result from open doses could lead to the inappropriate use of implanted systems for chronic opioid delivery, with the attendant questionable efficacy, morbidity and economic implications.

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CASE REPORT

Reversible renal failure following opioid administration

S. A. HILL, K. QUINN, M. P. SHELLY AND G. R. PARK

Summary

A patient who received intravenous papaveretum during and after operation developed anuria and biochemical evidence of impaired renal function in the first 6 hours after surgery. Administration of naloxone 0.4 mg was associated with a sustained improvement in urine output. Mean arterial pressure did not change significantly. The impairment of renal function may have been related to high plasma concentrations of codeine, one of the constituents of papaveretum.

Key words

Kidney; anuria.
Analgesics; papaveretum.

Administration of opioid drugs has been associated with a reduction in urine output in both experimental animals and man, although the exact mechanism whereby this occurs is unclear. In man, opioid abuse has been associated with both acute and chronic renal failure. There has been a report of two patients in whom dihydrocodeine in therapeutic doses precipitated acute renal failure which was reversed by the use of the specific opioid antagonist naloxone.[1] In this report we present a patient in whom papaveretum (a variable mixture of opioid including morphine 47.5–52.5%, codeine 2.5–5%, noscapine 16–22% and papaverine 2.5–7%) given for sedation and analgesia after aortic surgery was associated with impaired renal function which improved after treatment with naloxone.

Case history

A 60-year-old male was admitted to the intensive care unit for artificial ventilation after elective aortic aneurysmectomy, which did not involve the renal arteries, with a 2.2 litre blood loss. Analgesia was provided during operation by intravenous administration of papaveretum 20 mg; after operation, a total of 30 mg of papaveretum was given during the first 6 hours. There were no periods of intra-operative hypotension and postoperative hypertension was controlled with an infusion of sodium nitroprusside. Despite a mean arterial pressure (MAP) greater than 100 mmHg the patient remained anuric for 6 hours. An infusion of dopamine, at a low dose, had been used throughout the peri-operative period to provide renal protection and there was no response to intravenous frusemide administration. Postoperatively, the plasma urea concentration increased from a pre-operative value of 6.8 mmol/litre to 12 mmol/litre and plasma creatinine concentration increased from 135 μmol/litre to 341 μmol/litre, reflecting poor renal function. Six hours after operation the patient was unresponsive to painful stimuli and therefore naloxone 0.4 mg was given as a slow intravenous injection which produced an improvement in his conscious level. In addition, an increase in urine output was noted without any change in MAP, central venous pressure or other therapy (such as fluid administration). No further doses of naloxone were required as urine output, once established, was maintained with the administration of dopamine and frusemide. Analgesia was provided subsequently with sublingual buprenorphine.

Blood and urine samples were collected before and after naloxone treatment for subsequent analysis of codeine, morphine, morphine-3-glucuronide (M3G) and morphine-6-glucuronide (M6G) concentrations. Blood samples were collected into tubes containing lithium heparin as an anticoagulant and centrifuged at 3000 rpm for 15 minutes. The supernatant plasma was separated and stored at −20°C together with the urine samples before analysis for codeine,

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Table 1. Urine output and concentrations of opioids in urine and plasma after intravenous 0.4 mg naloxone at time t = 0.

Time (hours)		Urine output (litre) Last hour		Total
0		0.00		0.00*
16		0.12		1.00
36		0.15		2.17
		Plasma concentration (ng/litre)		
	Morphine	M3G	M6G	Codeine
0	1.04	0.77	0.37	—
16	0.29	0.48	0.90	3.34
36	0.70	0.21	1.81	0.78
		Urine concentration (ng/litre)		
	Morphine	M3G	M6G	Codeine
0	—	—	—	—
16	2.18	9.52	28.13	0.00
36	4.14	8.39	9.12	0.07

M3G, morphine-3-glucuronide, M6G, morphine-6-glucuronide.
*The patient was anuric for the first 6 postoperative hours before naloxone administration.

morphine, M3G and M6G using previously described techniques.[1,2] The results of these analyses and the changes in urine output are shown in Table 1.

Discussion

This patient received papaveretum for analgesia in the peri-operative period and subsequently developed acute renal failure. This is a well recognised complication of major aortic surgery and is attributed usually to episodes of hypotension, which did not occur in this patient. An increase in urine output was seen after the intravenous administration of the specific opioid antagonist naloxone, and was accompanied by an improvement in renal function as indicated by the increased clearance of codeine and morphine metabolites. Plasma concentrations of morphine and its metabolities were high. Initially, the concentration of morphine decreased, and then it increased. Plasma concentrations of M3G and codeine decreased after the diuresis, whilst those of M6G increased. The increase of morphine seen at 36 hours may represent metabolism of M6G back to morphine. Urinary concentrations of morphine and its metabolites were many times higher than the plasma concentrations. The decrease in the urinary concentration of M6G in the presence of an increased plasma concentration is surprising. It may be due to competition for the excretory mechanism by other substances, possibly explaining why the plasma concentrations increased.

The mechanism of opioid-induced antidiuresis is unclear and species differences occur. In the dog and rat, opioids stimulate vasopressin release. This does not seem to be the case for man.[3] The difference in the ratio of plasma : urine concentrations of morphine and its metabolites compared with codeine results in a high concentration of codeine remaining in blood, and this in turn results in impairment of renal function.

Opioid metabolites rather than the parent drug may be involved in inducing renal impairment, since metabolities accumulate in renal failure. Opioid metabolism in man occurs in the liver and little morphine is metabolised in the absence of liver function.[4] Thus renal impairment itself will not reduce opioid metabolism, but will impede metabolite clearance.[5,6] Whether renal impairment affects the excretion of all metabolites in the same way is unknown. If there is a difference, then individual metabolites may be affected in differing ways, as appears to be the case in this patient; morphine-3-glucuronide appeared to be excreted well, whilst morphine-6-glucuronide was excreted less effectively.

Similar improvement in renal function has been observed in two other patients treated with naloxone where papaveretum-induced renal impairment was suspected. This suggests that in some patients the administration of opioid drugs may induce deterioration of renal function sufficiently to precipitate renal failure. Should such an occurrence be suspected then treatment with naloxone appears to reverse the effect.

Acknowledgments

We wish to thank the nursing staff of the John Farman Intensive Care Unit for their help.

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CASE REPORT

Transient blindness following epidural analgesia

R. A. VICTORY, P. HASSETT AND G. MORRISON

Summary

A 43-year-old woman was given an epidural injection of steroid mixed with local anaesthetic, under general anaesthesia, for treatment of low back pain. In the recovery room she complained of blindness in one eye. Fundoscopy revealed retinal and vitreous haemorrhages in both eyes. Retinal haemorrhages can be caused by an increase in intracranial pressure and are therefore a possible complication of epidural anaesthesia.

Key words

Anaesthetic techniques, regional; epidural.
Complications; blindness.
Eye; blindness, retinal haemorrhages.

Epidural analgesia is commonly used in the management of patients with back pain. Occasionally it is necessary to perform this procedure under general anaesthesia, because of severe pain, but this makes it more difficult to detect any complications of the epidural injection. Changes in epidural pressure are directly transmitted to the cerebrospinal fluid. If significant increases occur, the associated rise in intracranial pressure may cause retinal haemorrhages secondary to a rise in retinal venous pressure. This is the first case report of temporary blindness caused by retinal haemorrhages, which may have been the result of the epidural injection.

Case history

A 43-year-old woman was referred for treatment of her back pain with epidural analgesia. She had an 8-year history of low back pain and investigations had showed degeneration of two lumbar discs. She had been given epidural analgesia under general anaesthesia one year previously and this had provided a few months of pain relief. She suffered from no other medical problems. It was decided to perform the epidural under general anaesthesia because she had severe pain. Anaesthesia was induced with thiopentone 350 mg and maintained with nitrous oxide in oxygen and isoflurane 2%. An 18-G Tuohy needle was used to inject bupivacaine 0.25% 40 ml containing hydrocortisone 200 mg into the epidural space over a period of 2 minutes. Anaesthesia was uneventful, but in the recovery room she complained that she could not see with her right eye and an ophthalmic surgeon was consulted. Fundoscopy revealed retinal, preretinal and vitreous haemorrhages in both eyes and in the right eye the macula was obscured.

She was given no treatment, but the retinal haemorrhages were monitored in the outpatient department. Six weeks later the visual acuity in her right eye was virtually normal. Her prognosis is excellent and a full recovery is anticipated.

Discussion

Visual disturbances are fairly common in the postoperative period[1] but most are mild and of no consequence; for example, blurred vision after atropine or diplopia as a result of inadequate reversal of neuromuscular blockade. An acute loss of vision, as occurred in this case, is more alarming and it could be from any one of a number of causes. Transient blindness has been described after ketamine[2] and in association with glycine absorption during prostatic resection.[3] Retinal artery occlusion[4] and corneal oedema[5] have also caused loss of vision after anaesthesia.

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In our patient the blindness was because of retinal haemorrhages, one of which involved the macula of the right eye. Retinal haemorrhages have been reported after laparoscopy and tubal insufflation performed in the Trendelenburg position, in a patient who had general anaesthesia, tracheal intubation and intermittent positive pressure ventilation.[6] In contrast, our patient was breathing spontaneously and had received an epidural injection, therefore the most likely cause was an increase in retinal venous pressure, which can occur if large volumes of fluid are injected rapidly into the epidural space.[7] It has been shown that an increase in epidural pressure is directly transmitted to the cerebrospinal fluid, and this in turn will cause a rise in intracranial pressure.[8] A significant increase in intracranial pressure may obstruct venous return and it has been suggested that retinal haemorrhages result from the associated rise in retinal venous pressure.[9] In a patient with a head injury, an epidural injection of 10 ml was sufficient to cause a large rise in intracranial pressure.[10] However, even in a patient with normal intracranial pressure, 10 ml of solution, if injected rapidly, can cause an increase in pressure.[11] The mechanism is similar to that in the Valsalva retinopathy, which can occur secondary to coughing or straining during emergence from anaesthesia.[12] However, in our case, nothing had occurred which would have caused a rise in intrathoracic pressure.

Most cases of retinal haemorrhage are asymptomatic, since patients will be unaware of visual disturbance unless the macula is involved. No treatment is required, unless massive haemorrhage involves the vitreous.

This case illustrates a further complication of epidural analgesia and provides another reason for giving epidural injections slowly.

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Anaesthesia, 1991, Volume 46, pages 942–945

CASE REPORT

A case of malignant hyperthermia?

A. A. BROEKEMA, G. A. BOERSMA AND P. J. HENNIS

Summary

An acute episode of a malignant hyperthermia-like syndrome is described which occurred after suxamethonium and isoflurane anaesthesia in a 41-year-old healthy male patient undergoing a minor elective hand operation. Dantrolene therapy rapidly reversed the life-threatening signs. Laboratory results appeared to confirm the suspicion of malignant hyperthermia. However, the in vitro contracture test, which was carried out according to the standards of the European Malignant Hyperthermia Group, was equivocal.

Key words

Anaesthetics, volatile; isoflurane.
Hyperthermia; malignant.
Neuromuscular relaxants; suxamethonium.

Malignant hyperthermia (MH) is a dangerous complication of anaesthesia. The combination of suxamethonium and a potent volatile anaesthetic agent can act as a trigger, but MH is not frequently associated with isoflurane anaesthesia. In 1982 the first case of MH after isoflurane anaesthesia was described; however, it was not confirmed by a positive *in vitro* contracture test.[1] Since then six more cases have been reported, three of whom were confirmed by a positive test.[2]

Case history

A 41-year-old male patient, weighing 85 kg presented for a local excision of a tumour on the radial side of his left wrist. He had undergone two previous anaesthetic procedures without any complication and was assessed as ASA 1. No premedication was given. After insertion of an intravenous line, an interscalene brachial plexus block was performed with 40 ml bupivacaine 0.375% and adrenaline 1:400 000. Anaesthesia, as assessed by pinprick 20 minutes after the injection, appeared to be adequate. However, at skin incision, this proved not to be so, therefore the patient was anaesthetised with thiopentone 425 mg and given suxamethonium 100 mg to facilitate intubation of the trachea. The anaesthetist noticed that the muscles of the neck were rigid, but tracheal intubation was uneventful. Controlled ventilation of the lungs was instituted (Dräger: Ventilog 2) and carbon dioxide (CO_2) output monitored by capnography (Datex). Anaesthesia was maintained with 30% oxygen in nitrous oxide and isoflurane 1% and a bolus dose of fentanyl 0.15 mg was given. Five minutes after intubation a rapid rise in the end-tidal CO_2 was noticed (7.8%) despite apparently adequate ventilation. Auscultation of the lungs and ventilatory pressures were normal, expansion of the chest wall was symmetrical and there were no signs of any leak of gas from the breathing system. The ventilator and the capnograph were checked and no defects were found. In 15 minutes the end-tidal CO_2 increased from 4.1% to greater than 10% (Fig. 1). The heart rate increased to 129 beats/minute, but the blood pressure remained stable. There was no cyanosis and pulse oximetry showed an oxygen saturation of 97%. Blood gas analysis 30 minutes after the induction of anaesthesia revealed a respiratory acidosis (pH 7.11; $Pa\text{CO}_2$ 10.4 kPa). Although the temperature of the skin felt normal, MH was suspected. Isoflurane was discontinued and the patient's lungs were hyperventilated with 100% O_2 with a clean ventilator and a fresh breathing system. The ventilation was increased to 18.5 litres/minute. A nasopharyngeal temperature probe was inserted and showed 37.5°C. However, within 15 minutes the temperature was 38.5°C and 10 minutes later it reached a peak of 39.2°C. By this time the patient was sweating profusely and felt extremely warm. Sodium bicarbonate 4.2% 250 ml was infused to prevent a metabolic acidosis. After dantrolene sodium 50 mg was given the end-tidal CO_2, temperature and heart rate decreased and after a total dose of 200 mg they were completely normal (Fig. 1). A urinary catheter was inserted

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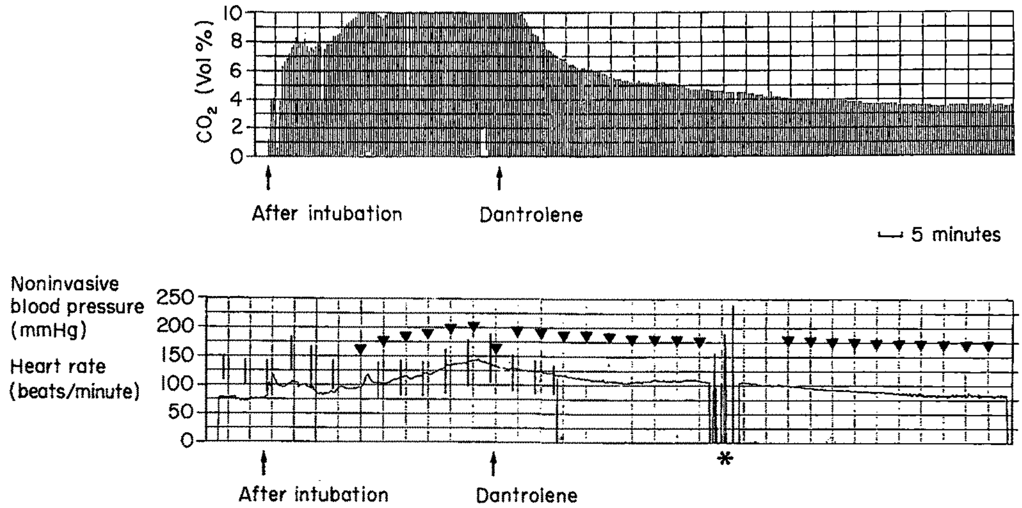

Fig. 1. Recordings of end-tidal CO_2 (upper panel), heart rate (——), noninvasive bloodpressure (|) and nasopharyngeal temperature ▼ (lower panel) *artefact.

and a diuresis was forced with frusemide 80 mg and mannitol 20% 100 ml to prevent tubular necrosis. This resulted in a urine output of 400–600 ml/hour. Surgery lasted 50 minutes. Intermittent positive pressure ventilation was continued and the patient was transported to the intensive care unit. Arterial blood gases, serum potassium and sodium were measured. The serum potassium was slightly elevated, but did not increase further. The creatine kinase (CK) and myoglobin concentrations in both serum and urine were increased (Fig. 2); the urinary concentration of myoglobin was 35 000 μg/litre. Serum creatinine was also increased, but returned to normal 6 hours later. Serum lactate dehydrogenase (LDH), serum aspartate aminotransferase (AST) and serum alanine aminotransferase (ALT) were increased (Fig. 3). The urine was kept alkaline to prevent tubular necrosis. Seven hours after the operation the tracheal tube was removed. The patient's temperature remained normal and the next day he returned to the ward, after which his recovery was uneventful. A detailed discussion with the patient took place. There was no family history of anaesthetic problems and the patient's two previous operations were apparently uneventful. In 1984 he underwent a vasectomy in another hospital under general anaesthesia. Premedication consisted of atropine and papaveretum. Anaesthesia was induced with thiopentone and pethidine and maintained by mask ventilation (Bain system) with 33% oxygen in nitrousoxide and halothane 1–2%. Surgery lasted 35 minutes and was uneventful. The second operation, a biopsy of the tumour of the left wrist, took place in our hospital a week before the present operation. A successful supraclavicular block was performed using 40 ml mepivacaine 2% with adrenaline 1:400 000.

The patient was discharged from hospital 5 days after the operation. Biochemical investigations were carried out, initially twice-weekly in outpatients and, after a month, at regular intervals by the general practitioner who informed us of the results. Two weeks after discharge from hospital LDH, ALT and AST had decreased and were approaching the moderately elevated pre-operative values (Fig. 3). Renal function remained unimpaired. Myoglobin was not detectable in the urine after 3 days, but serum levels were still elevated (1100 μg/litre) after 7 months. The CK remained high (Fig. 2) and even after 7 months it was 756 units/litre.

Four months after the operation a muscle biopsy was

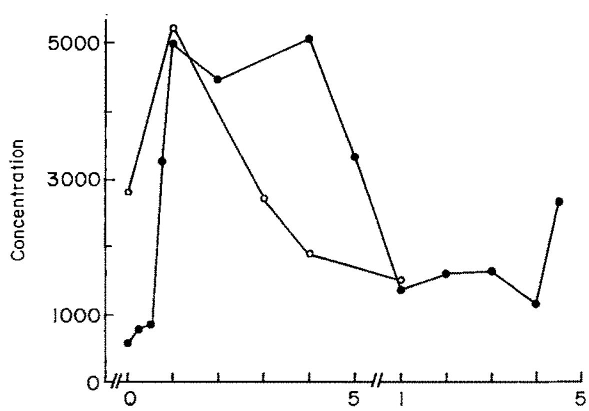

Fig. 2. Serum concentrations of myoglobin; μg/litre (○) and creatine kinase; units/litre (●).

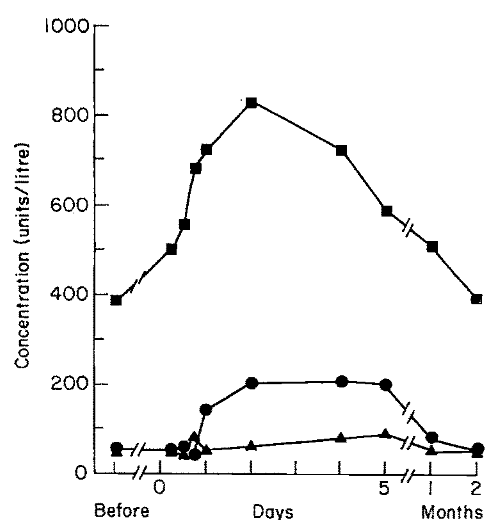

Fig. 3. Serum concentrations of lactate dehydrogenase (LDH, ■), aspartate aminotransferase (AST, ●) and alanine aminotransferase (ALT, ▲).

performed according to the standards of the European MH Group, under regional anaesthesia (a 3-in-1 lumbar plexus block). The *in vitro* contracture test was equivocal. Histopathological examination revealed that the muscle was not completely normal, but showed no 'classical' myopathy.

Discussion

Although MH-susceptible patients may have undergone previous anaesthetics with known trigger agents uneventfully, they can develop the signs of MH at any time.[2] This patient had received one anaesthetic with halothane. Stress may provoke MH, but this is a controversial subject.[3-5] In this case the patient did not receive premedication and had an unsuccessful brachial plexus block, therefore this might have induced a stress-reaction.

The early signs of MH are an increase in end-tidal CO_2, acidosis and a tachycardia.[6-8] Several studies have shown that the coincidence of masseter spasm with muscle biopsy-proven MH is about 50% in children.[9,10] In adults it is about 25%.[11-13] An increase in body temperature is a relatively late sign, so capnography is of crucial importance in detecting MH at an early stage.[6,9] An increase in temperature, myoglobinuria and an elevated serum creatine kinase are indicative of MH.[11,14]

The rapid response to dantrolene would seem to confirm the preliminary diagnosis; however, it does not prove MH.[15] In a recent study by Hackl *et al.*,[11] eight signs, which occurred during apparent clinical episodes of MH, were compared retrospectively with the results of the *in vitro* contracture test. The predictive value of the most informative signs, when combined, was only 78% specific for MH. However, two signs were not evaluated; the rise in end-tidal CO_2 and acidosis.

Dantrolene sodium is the only effective treatment for MH. The recommended dose is an initial bolus of 2.5 mg/kg intravenously, with a maximum cumulative dose of 10 mg/kg.[16-18] Further treatment is symptomatic; discontinuation of the volatile agent, hyperventilation with 100% oxygen through a fresh anaesthetic system, correction of acidosis and biochemical abnormalities, cooling and forced diuresis, for renal protection. A rapid cessation of surgery is recommended. The patient should be closely observed postoperatively in an intensive care unit for at least 24 hours, since MH may recur.[7,9]

Until now, the caffeine and halothane contracture tests on muscle are the only tests with which the diagnosis of MH may be confirmed or refuted.[19-22] The muscle biopsy can be safely performed in patients suspected of MH using a regional anaesthetic technique such as a 3-in-1 lumbar plexus block.[23] Since 1984, the tests have been standardised according to the European MH group.[19] In this case, it is not clear why the result of the muscle biopsy was equivocal. However, according to the literature, 15% of the patients suspected of having MH on clinical grounds have a MH-equivocal result.[21,22] Newer tests are being developed, but are not yet available in clinical practice.[2,14,20,22,24,25]

The clinical signs and the biochemical results are indicative of MH. However, the partial and prolonged recovery of the elevated CK and myoglobin is unusual. In most cases of MH these biochemical disturbances return to normal within a few weeks of the crisis.[26] This prolonged recovery time may indicate pre-existing neuromuscular disease, but histopathological investigation showed no 'classical' myopathy in this patient.

In conclusion, we believe that, despite the equivocal *in vitro* contracture test, the clinical manifestations during general anaesthesia, accompanied by severely disturbed biochemical changes, strongly suggest that this patient did suffer an MH crisis.

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Anaesthesia, 1991, Volume 46, pages 946–947

CASE REPORT

Extradural analgesia and previous spinal surgery

A radiological appraisal

M. A. CALLEJA

Summary

Extradural block was performed in a nulliparous patient with previous spinal surgery. Epidurographic evidence explains the rapid onset and extensive sensory block obtained.

Key words

Anaesthetic techniques, regional; extradural.
Surgery; spinal, laminectomy.

Case history

A 31-year-old nulliparous woman was admitted in early labour. Initially intermittent inhalation of Entonox was used for analgesia, followed by a dose of pethidine 100 mg intramuscularly. Neither provided satisfactory analgesia. The woman had been advised against extradural analgesia by her general practitioner because of previous spinal surgery. The duty obstetric anaesthetist was asked to assess her analgesic requirements.

A laminectomy had been performed 3 years previously at the L_{4-5} level, and the intervertebral disc removed. Preceding symptoms had consisted of severe back pain and numbness in the L_5 dermatome. A pre-operative myelogram had confirmed nerve root compression. The woman had made a good recovery from surgery with no recurrence of symptoms.

Her labour pains were mainly abdominal in distribution with a frequency of 5–7 minutes. Examination of her back showed a linear midline scar extending from the dorsal spine of L_2 to the spine of L_5. Extradural analgesia was not thought contraindicated.

An intravenous preload of 1000 ml 0.9% saline solution was administered. The extradural space was identified at T_{12}–L_1 and a 16 gauge extradural catheter advanced 4 cm cephalad into the space without difficulty. A test dose of 2% lignocaine 2 ml was given in the sitting position. After 5 minutes absence of motor block was confirmed (hip flexion was unimpaired), and the absence of hypotension noted.

Altered sensation to cold was noted in T_{12}–L_2 dermatomal distribution but the changes were equivocal. Significant pain relief was, however, obvious. 0.5% plain bupivacine 4 ml was administered with the patient in the left lateral position. After 10 minutes, sensory block extended from T_8 to L_4. No hypotension was noted. Over the next 4.5 hours additional 4 ml doses of 0.5% bupivacaine were administered by the attending midwife. Normal delivery proceeded uneventfully.

The extradural catheter was left *in situ* after delivery. Epidurograms were performed the following morning. Aqueous iohexol solution 4 ml was injected through the catheter with the woman in the left lateral position.

Figure 1 shows contrast medium in the extradural space down to the level of L_{4-5} (arrowed). No contrast medium is visible below that level. Figure 2 shows contrast medium in the thoracic extradural space. Most of the contrast medium reaches T_{8-9} level (solid arrow), but some contrast medium is visible up to the level of T_6 (open arrow).

Discussion

Previous spinal surgery is sometimes considered a relative contraindication to extradural analgesia. The reasons for this include: technical difficulty in identifying the extradural space, asymmetric spread of local anaesthetic solution and the possibility of a recurrence of back symptoms. The last may of course be unrelated to extradural analgesia, but this may be difficult to ascertain with certainty. Recent work has suggested that extradural block may be more difficult to establish in patients with previous spinal surgery, but with care may still be successful.[1,2]

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Fig. 1. Epidurogram showing spead of contrast medium to level of L_{4-5} (arrowed).

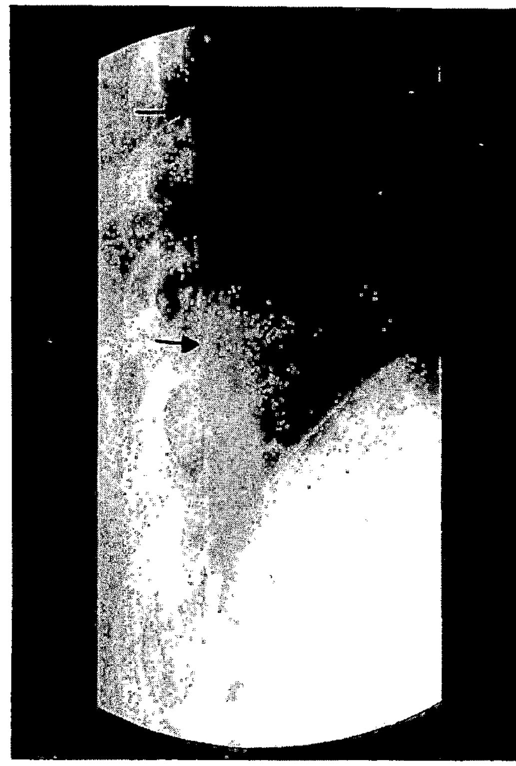

Fig. 2. Epidurogram showing spread of majority of contrast medium to T_{8-9} level (solid arrow) with additional minor spread to T_6 (open arrow).

In this patient, extradural analgesia was only considered after failure of alternative methods of analgesia. The risks and possibility of a failed or inadequate block should be discussed with the patient, but a rational (and legally valid) evaluation of risk may be difficult for a distressed parturient in pain. A commonsense approach is necessary. Unusual features of this case are: the rapid onset of analgesia, within 5 minutes of administering a test dose, and the relatively high block obtained (T_8). Both can be explained by the epidurographic evidence.

In the normal extradural space local anaesthetic solution is free to travel up and down the space. Some is invariably lost to the caudal extradural space. The pain of early labour is transmitted by pathways entering the spinal cord at the 11th and 12th dorsal segments. A dose of 2 ml of 2% lignocaine was ideally placed to block these segments. Doughty[3] has recommended a selective segmental block at T_{11-12} to reduce the incidence of forceps deliveries.

The spread of solution into the mid thoracic extradural space can also be explained by the absence of caudal loss of local anaesthetic, the anatomical block to spread at L_{4-5} prevents such loss (Fig. 1).

It is worth noting that hypotension was not a problem. This may be explained by the relatively small amount of contrast medium seen in the higher thoracic segments. Larger top-up doses may have resulted in hypotension. Preloading may have helped prevent hypotension. Also of note is the absence of sacral block. The performance of a caudal extradural or subarachnoid block would have been necessary if sacral block was required in the second or third stages of labour.

In conclusion, it is possible to provide adequate extradural analgesia during labour in women with previous spinal surgery. Postdelivery epidurograms may be useful in women who plan to have more children. Alterations in dose and technique may be necessary according to individual requirements and the anatomical level of spinal pathology.

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Anaesthesia, 1991, Volume 46, pages 948–951

APPARATUS

A low-flow to-and-fro system

Laboratory study of mixing of anaesthetic and driving gases during mechanical ventilation

M. Y. KADIM, G. G. LOCKWOOD, M. K. CHAKRABARTI AND J. G. WHITWAM

Summary

The insertion of a long deadspace tube between an anaesthetic breathing system and a ventilator produces only imperfect separation of the breathing system gas from the driving gas. This laboratory study has investigated different connecting tubes to establish the maximum tidal volume possible before ventilator gas contaminates the gas in a low-flow to-and-fro system (fresh gas flow 1 litre/minute). A larger volume tube enables the use of larger tidal volumes, and plastic corrugated tubes are slightly better than black rubber corrugated tubes in this respect. The maximum tidal volume possible without contamination decreases as ventilatory rate increases, but the maximum minute volume is increased. A 22 mm plastic corrugated tube of internal volume 1.5 litres should be adequate for clinical use with the to-and-fro system described in this study at a fresh gas flow of 1 litre/minute.

Key words

Equipment; breathing systems, absorbers.

The 'gas piston' technique has been used for mechanical ventilation of a circle system[1–3] and a rebreathing system.[4] It requires the insertion of a tube, which we term the ventilator-anaesthetic system connector (VASC), between the ventilator and the breathing system to prevent mixing of the anaesthetic gas and the driving gas. Such attachments have been available commercially for years; one example is the deadspace tubing unit marketed by Blease Medical Company for attaching the Manley 4 Mk II ventilator to a circle system. It has been shown that, even if the VASC volume is greater than the tidal volume, mixing between driving gas and fresh gas occurs and depends on (1) VASC volume, (2) ventilatory rate, (3) fresh gas flow (FGF) and (4) tidal volume (V_T). There are no reports of the use of a gas piston in a low-flow to-and-fro system.

We have undertaken a laboratory investigation of mixing between the FGF supplied to a to-and-fro system and the driving gas from the ventilator. Furthermore, because previous papers[2,3] on this subject have used corrugated tubes with standard 22 mm connections but differing in their volume per unit length, we have also evaluated the performance of two commonly available corrugated tubes as VASC.

Method

A Manley lung ventilator performance analyser[5] was used as a model lung, with a resistance of 5 cmH_2O/litres/seconds and a compliance of 50 ml/cmH_2O. We used a valveless ventilator that has been described in detail elsewhere.[6] It consists in essence of a high-pressure oxygen jet in the distal limb of a T-piece, directed towards the patient. An electronically timed solenoid valve switches the jet on to effect inspiration, and it functions as a constant pressure generator. The tidal volume is measured during the expiratory phase by the ventilator which automatically allows for the FGF during that period.[7]

The ventilator was connected to the model lung via the following (Fig. 1): a VASC of either corrugated plastic disposable tubing 22 mm in internal diameter (Intersurgical, Twickenham) or black rubber corrugated tubing (BOC), and with an approximate internal volume of 500 ml, 1000 ml, 1500 ml, or 2000 ml; a soda lime canister 5 cm in diameter and 9 cm long, containing 160 g of 4–8 mesh size soda lime (Durasorb, MIE); a T-piece for delivery of fresh gas; a catheter mount with a heat and moisture exchanger (Edith, Engstrom) to act as a dust trap; a sampling port for the gas analyser (Capnomac, Datex);[8] and a 9 mm internal diameter, 24 cm long tracheal tube (Portex). The Capnomac was calibrated using a standard gas mixture (Quick Cal, Datex). The volumes of the air space in the charged canister, and in the T-piece with its connections, were 100 ml and 40 ml respectively (as measured by water displacement at 20°C). With the Edith heat moisture exchanger, the volume of the three pieces connected together was 200 ml.

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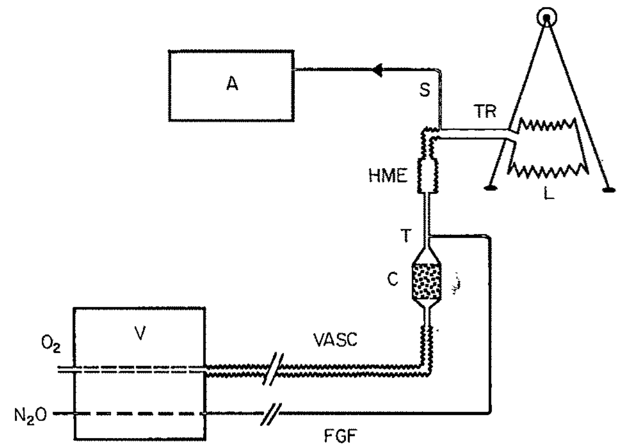

Fig. 1. The ventilator (V) is connected by a tubing (VASC) to a small soda lime canister (C). Fresh gas flow is fed from a flow meter through tubing (FGF) to a T-piece (T). A heat and moisture exchanger (HME) connects the T-piece to the tracheal tube (TR), attached to the lung (L). The gas analyser (A) samples from the junction of the heat and moisture exchanger and the tracheal tube through a sampling tube (S).

The system was ventilated using oxygen as the driving gas, and nitrous oxide as the fresh gas. An inspiratory to expiratory ratio of 1:2 was used throughout. A large V_T and an FGF of 10 litres/minute of nitrous oxide was used to flush the system until no oxygen was detected at the sampling port (see Fig. 1). The FGF and V_T were then reduced to 1 litre/minute and 100 ml respectively. The V_T was increased by 50 ml increments every 10 minutes until gas sampled at the end of one of these intervals contained 1% or more oxygen. $V_T$max denotes the largest V_T at which no oxygen was detected. Gas was not sampled continuously in order to prevent loss of system gas, but the gas which was sampled was not returned to the system to avoid contamination of system gas with air entrained by the Capnomac.

The above sequence was repeated for each of the eight VASC tested at ventilatory frequencies of 10, 15, 20, and 30 breaths/minute. The pressure at the model lung was noted at each V_T used. At the end of each experiment the catheter mount, the fresh gas and sampling ports were occluded, and the VASC was disconnected from the ventilator and sealed. Sufficient air from a gas syringe was then introduced to the system to reproduce the same pressure at the lung as had been noted during $V_T$max. Subtraction of this volume of air from the $V_T$max recorded at the ventilator gives the calculated $V_T$max achieved at the lung, allowing for compliance of the system and compressibility of gas (i.e. by deduction of compressible volume).

The Wilcoxon's signed-rank test was used to compare the difference between calculated $V_T$max achieved with the two types of VASC at all ventilatory rates and for all VASC volumes tested.

Results

The results are presented in Tables 1 and 2. The numbers in parentheses are the calculated values for $V_T$max at the lung. Table 1 shows $V_T$max at respiratory frequencies of 10, 15, 20, and 30 breaths/minute when using the plastic tubes as VASC. For all VASC volumes, $V_T$max decreased as frequency increased, and it can be seen that in all cases, increasing the frequency from 10 to 30 breaths/minute approximately halved the $V_T$max. At all ventilatory rates, $V_T$max increased with VASC volume; the $V_T$max achieved with a VASC volume of 2060 ml was approximately double that achieved with a 540 ml VASC at the same ventilatory rate.

Table 1. Plastic corrugated tubes as ventilator-anaesthetic system connectors (VASC).

Frequency (breaths/minute)	VASC volume (ml) 540	1050	1540	2060
10	500 (488)	700 (670)	750 (708)	850 (782)
15	400 (390)	550 (526)	600 (569)	750 (684)
20	350 (340)	450 (430)	500 (472)	650 (595)
30	200 (193)	300 (285)	350 (329)	450 (415)

Maximum measured expired V_T (ml) achieved before mixing of the fresh gas with driving gas when using four lengths of disposable translucent corrugated tube as VASC. The numbers in brackets are the calculated values of V_T at the model lung, i.e. after deduction of compressible volumes.

Table 2. Black rubber corrugated tubes as ventilator-anaesthetic system connectors (VASC).

Frequency (breaths/minute)	VASC volume (ml) 540	1030	1545	2060
10	400 (388)	650 (601)	700 (645)	800 (724)
15	350 (340)	500 (476)	550 (517)	750 (683)
20	300 (292)	400 (384)	450 (422)	600 (551)
30	200 (192)	250 (237)	300 (279)	400 (368)

Maximum measured expired V_T (ml) before mixing of the fresh gas with driving gas when using four lengths of black rubber corrugated tube as VASC. The numbers in brackets are the calculated values of V_T at the model lung, i.e. after deduction of compressible volumes.

Table 2 shows comparable results using the black rubber tubes. The same relation between $V_T$max and both respiratory frequency and VASC volume can be seen. $V_T$max was less than when using plastic tubes of equal internal volume. The median difference in $V_T$max between the plastic tubing and the black rubber tubing was 50 ml. This difference was statistically significant ($p < 0.001$), and the 95% confidence interval for the difference was 45–56.5 ml.

Figures 2(a) and 2(b) show the calculated minute volumes achieved before mixing of anaesthetic and driving gases when using the plastic and rubber tubes. These volumes increase with ventilatory rate but tend to plateau at the highest frequency used. It can be seen that the plastic tubes enable the use of larger minute volumes.

Discussion

Voss[1] made the first investigations into gas mixing when using the gas piston technique. He used a Bird Mark VIII ventilator to ventilate a circle system and rubber bag acting as a model lung with VASC of internal volumes 700 ml, 2000 ml and 3000 ml. His VASC had wide, smooth-bored lumens to encourage laminar flow within them, but he offered no evidence that they performed better than standard corrugated tubes of similar internal volume. Most of

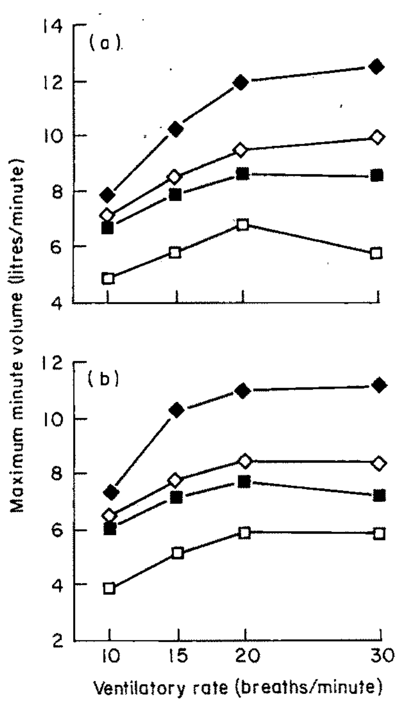

Fig. 2. The calculated maximum minute volumes achieved without mixing between the driving gas and the fresh gas during ventilation of a to-and-fro breathing system via different connector tubes (VASC) at ventilatory frequencies 10–30 breaths/minute. FGF is 1 litre/minute in all experiments. (a) Results for corrugated plastic VASC of internal volumes 540 ml (□), 1050 ml (■), 1540 ml (◇), 2060 ml (◆). (b) Results for corrugated black rubber VASC of internal volumes 540 ml (□), 1030 ml (■), 1545 ml (◇), 2085 ml (◆).

his work used high, fresh gas flows and is not comparable to the work presented here, apart from the data presented in Table 3. Linear interpolation between the calculated results in Table 1 shows that the $V_T$max achieved by Voss were about 100 ml less than ours. He also postulated the rule of thumb that, provided the V_T is less than the VASC volume, then $V_T$max equals the VASC volume times the FGF divided by six (all units in litres and minutes). Predictions based on this rule do not correlate well with the measured data in the present study.

Jeal[2] repeated Voss's work using more readily available components. He also ventilated a circle system with a rubber bag acting as model lung, using a Cyclator ventilator and a variable number of black rubber corrugated tubes as VASC, each being one metre. He argued that although the internal volume of these tubes was 510 ml, their functional volume was only 418 ml, a volume calculated by neglecting the corrugations, and that if this correction was taken into account, the smoothness of the VASC was immaterial. Ventilatory rates are not specified in Jeal's paper, but it can be seen that using a 3 m VASC (1500 ml) he achieved $V_T$max of about 250 ml at a minute volume of 5 litres, which is substantially less than the 422 ml reported here. It is interesting to note that Jeal found $V_T$max to depend solely on FGF and VASC volume, so that if these were fixed, the maximum minute volume was proportional to ventilatory rate. The finding is strikingly different to those of later workers. Jeal formulated another rule of thumb which is very similar to that proposed by Voss, i.e. the maximum V_T equals the VASC volume multiplied by the FGF divided by 6.3 (same units as Voss). This reflects a good overall agreement between the two studies.

Chakrabarti and co-workers[3] used the same ventilator as that in the present study to ventilate a circle system connected to a 4 litre rubber bag, using plastic corrugated tubing as VASC. Their results also showed that $V_T$max decreased as ventilatory rate increased. In the range of rates under consideration here, they found values for $V_T$max which were very similar to the results of the present study. This shows that the characteristics of the to-and-fro system, as regards mixing of driving gas with fresh gas, are comparable to a circle system.

Adams[4] used a Cape ventilator to ventilate a Penlon Bain system and a Manley lung ventilator performance analyser via a 530 ml corrugated tube. At 1 litre/minute FGF he achieved $V_T$max of 625 ml and 410 ml at rates of 13 and 30 breaths/minute. If the total VASC space is assumed to include the volume of the expiratory limb of the Bain system (660 ml) then the first of these results agrees with ours very well, but we found mixing at a lower V_T at the faster ventilatory rate.

Data from all these studies are presented for comparison in Table 3. It seems from our study and the last two studies discussed above[3,4] that the formulae given by Voss[1] and Jeal[2] underestimate the $V_T$max which can be used without mixing at the ventilatory rates and fresh gas flows used in this study.

Our experiments show that, volume for volume, the disposable tubing (longer per unit volume) performs better as VASC than the black rubber tube. Jeal's suggestion (that the volume of the tubes measured by water displacement is greater than their 'smooth' functional volume) is a plausible explanation for this difference, and is in keeping with

Table 3. A summary of relevant results from previous studies.

Source	VASC space (ml)	Ventilatory rate	Tidal volume (ml)	Minute volume (litres)
Voss[1]	700	17	300	5
	2000	25	400	10
Jeal[2]	1530	20	250	5
Chakrabarti *et al.*[3]	600	15	400	6
	600	30	200	6
	900	15	600	9
	900	30	300	9
Adams[4]	1190	13	625	8.3
	1190	30	410	12.3

A selection of results from different studies, each reporduced here because it was obtained under conditions comparable to those in the present study. FGF was 1 litre/minute in every case.

our results. A possible alternative explanation is that the narrower lumen better maintains the integrity of the mixing front between the anaesthetic and driving gases, and that the extra length of the plastic tubing provides greater spatial separation of the breathing system from this mixing front. In this case, further investigation might establish the best balance between the prevention of mixing with narrower tubes and the increased flow resistance that this incurs. We also prefer the plastic tube for its lighter weight, and in a clinical context it has an additional advantage in that it absorbs less volatile anaesthetic agent.

We have shown that by using a VASC of 1500 ml and a fresh gas flow of 1 litre/minute it is possible to achieve a minute volume of 8.9 litres at a rate of 15 breaths/minute without mixing of anaesthetic and driving gases. Radford's classic study[9] of ventilatory requirements predicts that, even allowing for increased physiological deadspace during anaesthesia, 8.9 litres will be enough to ventilate a 100 kg male to normocapnia. Seeley and his associates[10] have investigated ventilatory requirements under anaesthesia using a Bain system. At high fresh gas flows of more than 200 ml/kg/minute (i.e. sufficient to prevent rebreathing), the $P\text{aCO}_2$ was found to depend on minute ventilation. From his nomogram it can be seen that 80 ml/kg/minute ventilation achieved normocapnia ($P\text{aCO}_2$ 5 kPa), and 110 ml/kg/minute achieved mild hypocapnia ($P\text{aCO}_2$ 4 kPa). Even though we have used only 1 litre/minute FGF, the soda lime canister prevents rebreathing of carbon dioxide so that we can expect these values to apply to our system. Those values also predict that the ventilatory requirements of a patient of up to 100 kg are less than the 8.9 litres which can be met by this system without mixing of anaesthetic and driving gases.

It therefore can be concluded that if a 1500 ml VASC is used with the to-and-fro system described here, with a fresh gas supply as low as 1 litre/minute, then there will be no significant mixing between driving gas and anaesthetic gas when the system is applied in clinical practice using normal tidal volumes and ventilatory frequencies.

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APPARATUS

Evaluation of a small soda lime canister in a to-and-fro system

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Summary

The main disadvantages of the to-and-fro system (the bulky canister and the progressive increase in apparatus deadspace) may be overcome by the use of a smaller canister. In this laboratory study, we have evaluated a 160 g canister in a low-flow to-and-fro system (fresh gas flow 1 litre/minute). Two carbon dioxide productions of 150 and 200 ml/minute were simulated. The mean times to exhaustion, defined here as a 0.5 kPa rise in end-tidal $P\mathrm{CO_2}$, *were 112 and 79 minutes in the 150 and 200 ml/minute carbon dioxide groups respectively. Ventilation to normacapnia or hypocapnia did not affect the times to exhaustion. The soda lime absorbed 16 litres of carbon dioxide before exhaustion, and this was not affected by minute volume or carbon dioxide production. A small soda lime canister is suitable for carbon dioxide absorption in a low-flow to-and-fro system for ventilated adults.*

Key words

Carbon dioxide; absorption.
Equipment; absorbers.

Interest in closed and low-flow anaesthesia has continued since the introduction by Waters in 1924[1] of soda lime for absorbing exhaled carbon dioxide during anaesthesia. There have been several modifications on the soda lime absorber system over the years, such as the use of the circle system by Sword,[2] the various arrangements of the components of the circle system,[3] and the use of different sizes of soda lime canisters.[4,5] There is no recent study on the use of a small soda lime canister in a low-flow to-and-fro system. We have performed a laboratory evaluation of the performance of a 160 g soda lime canister in such a system, intending it for use in adults whose lungs are mechanically ventilated during anaesthesia.

Method

The experimental arrangement is illustrated in Figure 1. A Manley lung ventilator performance analyser[6] was used as a model patient, with a resistance of 5 $\mathrm{cmH_2O}$/litres/second and a compliance of 50 ml/$\mathrm{cmH_2O}$. We refer to this as 'the lung'. Carbon dioxide from a flowmeter calibrated against a dry spirometer (P. K. Morgan, Chatham, England) was fed into the bellows of the lung via a finely fenestrated catheter introduced through the pressure measurement port. The valveless ventilator of Chakrabarti and Whitwam[7] was connected to the lung via the following: a length of corrugated plastic tubing (Intersurgical, Twickenham) of internal diameter 22 mm and internal volume 2 litres, to prevent mixing between the driving gas from the ventilator and the fresh gas;[8] a cylindrical soda lime canister of internal dimensions 5 cm diameter and 9 cm length, containing 160 g of 4–8 mesh size soda lime (Durasorb, MIE); a T-piece for delivery of fresh gas; a catheter mount with a heat and moisture exchanger (Edith, Engstrom); a sampling port for gas analysis; and a 9 mm diameter, 24 cm long tracheal tube (Portex). A fresh gas flow (FGF) of 50% nitrous oxide in oxygen was measured through flow meters calibrated against a dry spirometer (P. K. Morgan, Chatham, England). Fresh soda lime was used for each experiment, and this was only tapped, not packed, into the canister. Sampled gas was analysed continuously by an infrared absorption device (Capnomac, Datex[9]) calibrated before each set of experiments using a standard gas mixture (Quick Cal, Datex). Analysed gas was returned to the system with the fresh gas flow. A pen-recorder (Lectromed Multitrace 4) was connected to the analogue output of the Capnomac to obtain a permanent record of measured carbon dioxide.

A FGF of 1 litre/minute and a tidal volume (V_T) of 650–680 ml was used in each of four experimental groups. In groups 1 and 2 a flow of carbon dioxide ($\dot{V}\mathrm{CO_2}$) of 150 ml/minute was introduced into the lung and the minute ventilation ($\dot{V}$) adjusted to achieve an initial end-tidal $P\mathrm{CO_2}$ of 5.3 kPa (group 1) and 4 kPa (group 2) by using ventilatory frequencies of 12 and 15 breaths/minute respectively. In groups 3 and 4 the $\dot{V}\mathrm{CO_2}$ was 200 ml/minute and the

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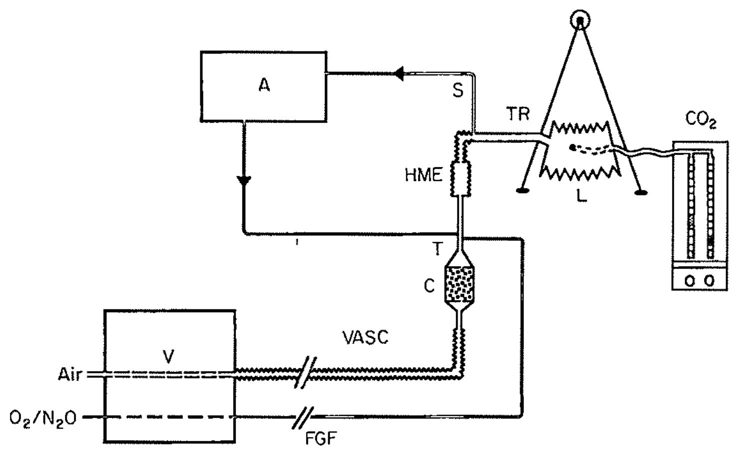

Fig. 1. The ventilator (V) is connected by a tubing (VASC) to a small soda lime canister (C). Fresh gas flow is fed from flow meter through a tubing (FGF) to a T-piece (T). A heat and moisture exchanger (HME) connects the T-piece to the tracheal tube (TR), attached to the lung (L). The gas analyser (A) samples from the junction of the heat and moisture exchanger and the tracheal tube through a sampling tube (S) and returns that gas to the T-piece as indicated by the arrow. Carbon dioxide is measured in a flow meter (CO_2) and fed into the lung through a finely fenestrated catheter.

ventilatory frequency adjusted to 16 and 20 breaths/minute to achieve again an initial end-tidal $P\text{CO}_2$ of 5.3 (group 3) and 4 kPa (group 4) respectively. Each experimental group comprised five identical individual experiments.

The times in minutes, taken for the end-expiratory and end-inspiratory $P\text{CO}_2$ to increase by 0.25 and 0.5 kPa were noted and termed $E_{.25}$, $E_{.5}$, $I_{.25}$ and $I_{.5}$ respectively.

We use the term absorption capacity (AC) of soda lime to denote the volume of carbon dioxide in litres at ambient temperature and pressure in dry gas (ATPD) that is absorbed per 100 g of soda lime before a given rise in end-tidal $P\text{CO}_2$ occurs. The AC is calculated at times $E_{.25}$ and $E_{.5}$ by multiplying that time (minutes) by the appropriate $\dot{V}\text{CO}_2$ (ml/minute) and dividing the result by 1600.

Analysis of variance and paired *t*-test were used for statistical analysis as appropriate.

The temperature of gas in the breathing system was measured at the junction of the tracheal tube with the catheter mount and at the junction of the T-piece with the soda lime canister, using Ellab (Copenhagen) MEA probes which have a small heat capacity and a rapid response time. The temperature of the outside of the canister was measured using a series of three Ellab MHF probes, attached by sticky tape along its length. All three probes were matched to within 0.4°C over the range 18–40°C. The experimental arrangement was unchanged except for the temperature probes inserted through small holes in the catheter mount. The holes were rendered gas-tight with small amounts of a proprietary sealant (Fernox LS-X). The experiments were conducted with $\dot{V}\text{CO}_2$ 200 ml/minute, FGF 1 litre/minute, V_T 600 ml and at a ventilatory rate 10 breaths/minute. Temperatures were noted every 10 minutes; when the temperature varied through the ventilatory cycle, the peak temperature was recorded.

The flow resistance of a charged canister was measured using a water manometer at an air flow of 30 litres/minute. The experiment was repeated seven times after recharging with fresh soda lime each time.

Results

The mean times to exhaustion of soda lime in groups 1–4 are presented in Table 1. The derived AC of soda lime in the same groups is shown in Table 2.

Inspiratory and expiratory $P\text{CO}_2$

In all the groups the mean times for inspiratory $P\text{CO}_2$ to rise to 0.25 and 0.5 kPa were longer than the mean times for

Table 1. The mean (SD) of times in minutes for the end inspiratory (I) and end expiratory (E) $P\text{CO}_2$ to rise to 0.25 and 0.5 kPa.

	$I_{.25}$	$E_{.25}$	$I_{.5}$	$E_{.5}$
Group 1 (n = 5)*	101 (4.2)	89† (5.5)	123 (2.7)	116‡ (2.2)
Group 2 (n = 5)	99 (7.4)	81† (5.5)	121 (7.4)	109‡ (2.2)
ANOVA: 1 vs 2		ns		
Group 3 (n = 5)	64 (7.4)	56† (4.2)	84 (9.2)	77‡ (7.6)
Group 4 (n = 5)	66 (7.4)	60† (5.0)	87 (7.6)	81‡ (6.5)
ANOVA: 3 vs 4		ns		
Group 1+2 (n = 10)	100 (5.8)	85† (6.7)	122 (5.4)	113‡ (4.3)
Group 3+4 (n = 10)	65 (7.1)	58† (4.8)	85 (8.1)	79‡ (7.0)
ANOVA: 1+2 vs 3+4		P < 0.001		

*$\dot{V}\text{CO}_2$ 150 ml/minute in groups 1 and 2, and 200 ml/minute in groups 3 and 4. Groups 1 and 3 normocapnic, groups 2 and 4 hypocapnic. FGF 1 litre/minute in all groups. Statistical significance using Student's *t*-test: † = p < 0.05 between $I_{.25}$ and $E_{.25}$ within group; ‡ = p < 0.05 between $I_{.5}$ and $E_{.5}$ within group.

Table 2. The mean (SD) absorption capacity (AC) for carbon dioxide in litres per 100 g of soda lime.

	AC at $E_{.25}$	AC at $E_{.5}$
Group 1 ($n = 5$)*	8.3 (0.5)	10.8 (0.2)
Group 2 ($n = 5$)	7.6 (0.5)	10.3 (0.2)
Group 3 ($n = 5$)	7.0 (0.5)	9.6 (1.0)
Group 4 ($n = 5$)	7.5 (0.6)	10.1 (0.8)
Group 1+2 ($n = 10$)	7.9 (0.6)	10.6 (0.4)
Group 3+4 ($n = 10$)	7.3 (0.6)	9.9 (0.9)
Anova	ns	ns

*$\dot{V}CO_2$ 150 ml/minute in groups 1 and 2, and 200 ml/minute in groups 3 and 4. Groups 1 and 3 normocapnic, groups 2 and 4 hypocapnic. FGF 1 litre/minute in all groups.
$E_{.25}$, $E_{.5}$: the times at which the expired carbon dioxide partial pressure reached 0.25 and 0.5 kPa respectively.

expiratory PCO_2 to reach the same levels and the differences were statistically significant ($p < 0.05$). The mean differences in these times at the 0.5 kPa end-point (i.e. $I_{.5}$–$E_{.5}$) were 7, 12, 7, and 6 minutes in groups 1–4 respectively.

Ventilation

Ventilation to 5.3 kPa or to 4 kPa did not affect the times to reach either end point of exhaustion, i.e. there were no statistically significant differences between groups 1 and 2 or between groups 3 and 4.

Carbon dioxide load

The data from groups 1 and 2 (VCO_2 150 ml/minute) were pooled together and compared with the pooled data from groups 3 and 4 (VCO_2 200 ml/minute). Increasing the carbon dioxide input from 150 to 200 ml/minute caused a reduction in mean $E_{.5}$ from 112.5 minutes to 79 minutes. Similar reductions were seen at all exhaustion points. These differences are statistically significant.

Absorption capacity

Table 2 shows the mean AC in each experimental group. There were no statistically significant differences attributed to ventilation or carbon dioxide input. The mean AC at $E_{.5}$ for all the groups was 10.2 litres.

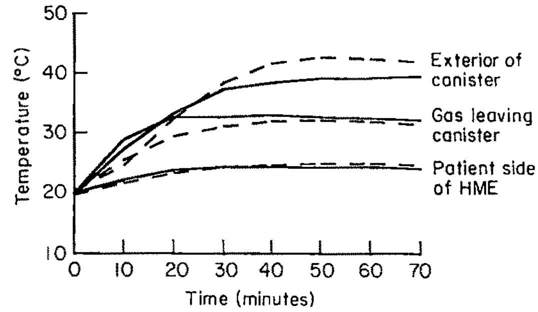

Fig. 2. The maximum temperature of the outside of the 160 g soda lime canister, of gas leaving the canister and of gas on the patient side of the heat and moisture exchanger (HME), plotted as functions of time. CO_2 production 200 ml/minute. The solid and dotted lines represent two separate experiments.

Temperature

The results of the temperature study are shown in Figure 2. In both experiments, the maximum temperature measured on the canister surface was in the middle, and only these values are shown. Temperature variations with the respiratory cycle were small on the lung side of the heat and moisture exchanger (HME), so that we regard these values as accurate. The variations in temperature recorded near the soda lime canister were too large for the digital readout to settle between cycles, and the peak readings reported here must be low.

Flow resistance of the canister

The flow resistance mean (SD) of the charged canister was 0.26 (0.03) kPa litres/second measured at a flow of 30 litres/minute.

Discussion

Absorption capacity and end points

Theoretically one gram molecular weight of calcium hydroxide (74 g) will absorb 44 g of CO_2 or 22.4 litres at standard temperature and pressure in dry gas (STPD). A gram molecular weight of sodium hydroxide (40 g) would

Table 3. Values of soda lime absorption capacity found in previous studies.

Study	System	End point	Soda lime mass (g)	CO_2 input (ml/minute)	Absorption capacity (litres)
Young[4]	circle	0.2%	2000	200	17.3
			1700	200	15.7
Jorgensen and Jorgensen[5]	circle	0.6%	600	300	18.0
			500	300	7.0
			400	300	3.2
			300	300	0.6
Andersen *et al.*[11]	Venturi	0.6%	300	150	19.2
			300	200	16.3
			200	100	18.8
			200	150	15.9
			200	200	15.5
			100	100	15.7
			100	150	10.9
			100	200	6.1
Ten Pas *et al.*[13]	to & fro	0.5%	550	320	2.6
	circle	0.5%	550	300	8.1

absorb 22 g CO_2 or 11.2 litres at STPD. In practice the absorption capacity may be 35%–85% of that value.[10] We have used Durasorb, which has a theoretical AC of 24.3 litres (MIE, personal communication).

Previous investigators have found that the exhaustion of soda lime during exposure to carbon dioxide is a gradual process[11,13] and therefore some respiratory carbon dioxide concentrations have to be taken as end-points to enable comparison between different studies. The end-point is an artificial but important factor that affects the AC. Other factors that affect the AC are the carbon dioxide load,[11] soda lime mass,[11] ventilatory variables,[12] and the type of breathing system used.[13] Table 3 shows values of AC from several studies.

We have taken rises of 0.25 and of 0.5 kPa in the end tidal $P\text{CO}_2$ as end-points because they are acceptable approximations to the 0.2%,[4] 0.5%,[13] and 0.6%[11] carbon dioxide concentration used by other investigators.

The effect of apparatus dead space

A major disadvantage of the to-and-fro system is the gradual increase in apparatus deadspace as the part of the soda lime nearer to the patient becomes exhausted.[13] Ten Pas and his associates have studied the ability of a 550 g canister in a to-and-fro system to absorb carbon dioxide from a model lung receiving a $\dot{V}\text{CO}_2$ of 320 ml/minute and ventilated at 20 breaths/minute with a tidal volume of 500 ml. The mixed inspiratory carbon dioxide concentration rose by 0.5% after 45 minutes while the end inspiratory carbon dioxide took 210 minutes to reach the same level. This is attributed to the conversion of the patient end of the soda lime canister into deadspace as the granules become exhausted. The end inspiratory gas has penetrated deeper into the canister, and thus has the lowest carbon dioxide concentration. They concluded that the end inspiratory carbon dioxide concentration should not be used as an indicator of the ability of soda lime to absorb carbon dioxide. They recommended that 1 hour to 1.5 hours was the limit for safe use of soda lime in a closed to-and-fro system in adults.

In this study the problem of increasing deadspace was overcome by using a smaller canister with an air space of 100 ml and by using a larger V_T of 650 ml. This meant that all the granules were in contact with almost all of the alveolar gas and so they became exhausted evenly. It is equivalent to just using the patient end of a Waters' canister: when the deadspace of the Waters' canister begins to increase, the small canister is exhausted. The end expiratory $P\text{CO}_2$ was used instead of mixed inspiratory carbon dioxide concentration because it could be measured directly and it reflects exactly the mixed inspiratory carbon dioxide concentration within a few breaths.[14] Using the 160 g canister presented in this study, the mean difference between the times for inspiratory and expiratory $P\text{CO}_2$ to rise to 0.5 kPa was only 10 minutes in groups 1 and 2 and 6.5 minutes in groups 3 and 4. These differences were statistically significant but very much less than the 165 minutes found by Ten Pas *et al.*[13] They are not clinically important.

The effect of soda lime mass

Increasing the soda lime mass in the absorber generally increases the AC.[4,5,11] For a circle system, Jorgensen and Jorgensen recommend 600 g as the minimum soda lime mass that provides effective absorption.[5] There are no recent studies that compare different soda lime masses in the to-and-fro system. The findings in this study show that a mass as small as 160 g is effective in providing carbon dioxide absorption for ventilated adults for one to two hours.

The effect of the breathing system

Adriani and Rovenstine[12] showed that the AC of soda lime was greater in the to-and-fro system than in the circle, but Ten Pas and his associates have shown the reverse.[13] Jorgensen and Hansen described a unique breathing system termed the 'Venturi system'[15] in which a Bain system is modified by the introduction of a constriction in the FGF inlet that entrains some of the expired gas through a soda lime canister. They attained large AC in 200 and 300 g masses of soda lime (Table 3) but required FGF of 30 ml/kg to operate the system. The low-flow system described here achieves an AC of 10 litres and requires less FGF which represents further economy of anaesthetic agents.

The effect of ventilation

Increasing minute ventilation by a fraction of one third did not affect the time to exhaustion or the AC in this study. These findings are in contrast to those of Adriani and Rovenstine in 1941[12] who found that a similar increase in ventilation nearly halved the time to exhaustion of a 500 g canister ventilated with a V_T of 500 ml. We cannot explain the differences but we notice that in the latter study the site and timing of sampling of respiratory gas were not specified.

The effect of carbon dioxide load

Carbon dioxide load was the only factor that affected the time to exhaustion of soda lime in our study. We have chosen the carbon dioxide inputs of 150 and 200 ml/minute to simulate patients weighing 75–100 kg under anaesthesia.[16] The AC was the same at both levels of carbon dioxide inputs showing that there was no added deleterious effect of a higher carbon dioxide input on the soda lime in this particular experimental arrangement other than a direct quantitative relationship.

Temperature

The peak temperature recorded on the exterior of the canister was not enough to be a risk to the patient; it is comfortable to hold at all times. The external temperature of a standard Waters' canister is greatest at the patient end,[12] but if the small canister is thought of as merely a truncated version of the standard one, it is no surprise that the hottest point of our canister was in the middle. The HME is such an effective temperature barrier that, although the patient's expired gas will be warmer than the gas in the bellows of the artificial lung, we do not expect this to cause the canister to get much hotter in clinical practice. The peak air temperatures measured near the canister are certainly falsely low: the fresh gas contributes to cooling of the probe during expiration, and the heat

content of the inspired gas is insufficent to raise the probe temperature to an equilibrium value in the time available. However, the HME will protect the patient from high temperatures in the breathing system gas, should they occur. Thus we are confident that the patient will be at no risk from any type of thermal injury.

Clinical application

Our results show that the relatively small mass of 160 g soda lime can be used effectively in a low flow to and fro system for 1 to 2 hours for an adult producing 150 to 200 ml/minute of carbon dioxide. This system is intended for use during controlled ventilation when large V_T can be assured and the work of breathing is carried out by the ventilator. Application of this system to spontaneously breathing patients would require that the apparatus dead space and the flow resistance be reduced to a minimum. The system lends itself to procedures that require ventilation for short periods of time (e.g. laparoscopies) in which the use of the traditional circle system would be slow and uneconomic. A disposable version would be suitable for use in the majority of adult anaesthetics.

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APPARATUS

Environmental contamination during tracheal suction

A comparison of disposable conventional catheters with a multiple-use closed system device

M. COBLEY, M. ATKINS AND P. L. JONES

Summary

The extent of airborne environmental bacterial contamination which occurs following tracheal suction has been investigated in patients undergoing intermittent positive pressure ventilation in the intensive therapy unit. Two methods of performing suction, one using a conventional open technique and one using a closed system (Stericath), have been compared. Significantly lower levels of environmental contamination were observed when the closed system was used.

Key words

Equipment; catheters, suction.
Infection; contamination, bacterial.

It is common for patients who undergo intermittent positive pressure ventilation (IPPV) in an intensive therapy unit (ITU) to receive regular tracheal suction. The conventional method of tracheal toilet requires that the breathing system is opened to atmosphere at the tracheal suction connector to permit the introduction of a sterile suction catheter by a sterile gloved hand. The catheter and the glove are discarded after single patient use in order to minimise bacterial contamination. It is usual for the function of the ventilator to be interrupted during the procedure. An aerosol of droplets of condensate and tracheal secretions can be seen clearly to be expelled from the connector during passive exhalation by the patient and during the positive pressure phase of ventilation by the machine. Ventilators which provide continuous positive airway pressure (CPAP) cause a continuous high flow of gas to be delivered from the open suction connector, and this tends to increase both the quantity and the range of resulting environmental contamination. It is reasonable to suppose that extensive contamination of the environment and the operator occurs directly as a result of the use of this method of tracheal suction.

The Portex Stericath is a closed tracheal suction system which has been developed to minimise environmental contamination (Fig. 1). The device consists of a T-shaped suction union which incorporates a re-usable suction catheter. The catheter is withdrawn into a flexible plastic film sleeve between successive suction procedures. The sleeve prevents contact between the catheter and the environment and permits the same suction device to remain in position in the breathing system for 24 hours before it is replaced. The tip of the catheter protrudes into the lumen of the catheter mount through a close-fitting flange. The catheter is grasped through its sleeve to advance it into the tracheal tube connector and on into the tracheobronchial tree. The flange provides a gas-tight fit around the catheter and prevents the loose-fitting sleeve from being inflated during IPPV. The flange wipes any secretions from the outer surface of the catheter as it is withdrawn. The catheter is fitted with a vacuum control valve which has a spring-biased piston action. This device must be compressed continuously to maintain suction. It effectively prevents suction from being applied continuously to the airways inadvertently. The devices which were used in this trial were provided with an irrigation port on the catheter mount. It was intended that irrigation fluid should be instilled through the port after the catheter had been withdrawn to a blue line mark which was just visible through the sheath. This fluid was aspirated through the catheter, by operating the suction valve, thereby washing it clear of accumulated secretions. The port has been relocated to the other end of the catheter in the currently available version of the device, which now includes a narrow second lumen within its wall. This lumen delivers irrigation fluid to the tip of the catheter.

The study investigated the difference in environmental

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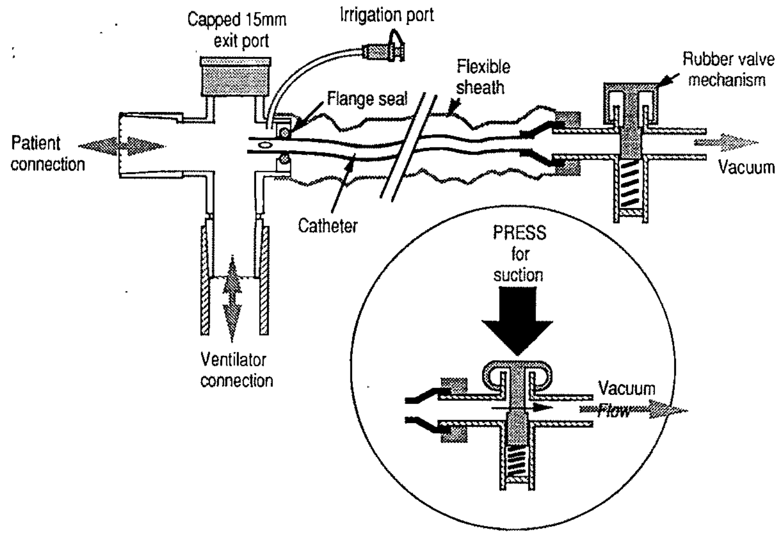

Fig. 1. The Portex Stericath.

contamination which occurred when the conventional and the closed tracheal suction techniques were applied.

Method

Eleven patients were investigated. Each was receiving IPPV through a tracheal tube and none was suffering from clinically overt respiratory infection. Consent for the investigation was not considered to be necessary because hourly suction and twice daily physiotherapy were part of routine treatment. Ethics committee approval for the study was obtained.

The respiratory tract of each patient was known to be colonised by a specific species of one of a number of Gram-negative bacilli which could be readily identified and differentiated from background flora in the ITU. Thus, each patient harboured an infecting organism which could act as a marker of environmental contamination. The organisms included *Escherichia coli, Pseudomonas aeruginosa, Enterobacter cloacae* and *Proteus* species. Only those patients who were considered on clinical grounds not to have a significant respiratory tract infection and were therefore unlikely to receive antimicrobial therapy during the trial period were included. Patients who received antibiotic therapy were withdrawn from the study. The environmental contamination was measured using two methods:

Air sampling. A Reuter centrifugal air sampler was placed 30 cm from and 10 cm above the suction port of the tracheal tube. The sampler held a nutrient agar strip over which the impelled current of air passed for a sampling period of 2 minutes. During this time a volume of 80 litres of air passes through the instrument.[1] The device is effective in collecting particles in the size range 4–20 μm.[2] A fresh agar strip was used for each sampling period. Samples were taken for the 2 minutes immediately before and the first 2 minutes after suction. The agar strips were incubated aerobically at 37°C for 48 hours and the number of colonies that had grown were counted. Only the patient and the investigator were within the sampling field during the sampling period. It is difficult to identify the individual marker colonies with this method because of the large number of other colonies which also grow, including the background flora of the ITU. For this reason, we looked only at the total number of airborne organisms grown before and after suction. This gave an accurate quantitative measure of the change in environmental contamination caused by either suction method.

Settle plates. Blood agar plates were placed at distances of 0.5, 1, 1.5 and 3 metres from the suction port. This means of sampling provides an effective method of collecting and identifying the marker bacillus from the respiratory tract of each subject. The plates were exposed for 20 minutes before and after suction. New dishes were used for each sample period. The plates were incubated aerobically at 37°C for 48 hours, when any colonies of the marker bacillus were identified by using colonial morphology, Gram staining, antibiotic sensitivity patterns and standard chemical tests.[3,4]

Sampling was undertaken on two successive days. On the first day, tracheal suction was undertaken four times at hourly intervals using the open technique. Thereafter, the Stericath was attached and suction was undertaken hourly for the next 4 hours using the closed technique. Bacterial sampling using the Reuter air sampler and the settle plates was repeated at each of the eight suction procedures. The Stericath remained in place for 24 hours, and was used for routine suction. No further environmental sampling was performed until the following day. On the second day, the order of procedure was reversed, with the closed method being tested for the first 4 hours, followed by the open technique for the second 4 hours. Presuction sampling proved to be impossible for reasons of protocol infringement on a number of occasions (16 of the possible 144). The post-suction sampling was omitted on all these occasions.

Sputum samples were taken on both days to ensure that no significant change in the marker bacillus composition of tracheal secretions had occurred during the study period. The number of Gram-negative bacilli in these specimens was calculated by inoculating 10 μlitre aliquots of serially diluted samples (with 0.5% N-acetyl-L-cysteine) on to horse blood agar and incubating for 48 hours at 37°C.

There is a potential risk of bacilli growing within the catheter sheath, which could cause autocontamination on repeated suction.[5] After removal of the Stericath, the protective sheath was opened under aseptic conditions and

Table 1. Total colony counts measured by air sampling before and after tracheal suction using open or closed suction systems.

	System	Sequence	Mean of subject means	SD
First day	Open	Before suction	40.2	22.7
		After suction	70.2	31.3
		Increment	+30.0	11.8
	Closed	Before suction	40.6	19.2
		After suction	48.7	19.9
		Increment	+8.1	5.1
Second day	Open	Before suction	31.0	14.3
		After suction	51.7	18.1
		Increment	+20.7	7.9
	Closed	Before suction	32.2	11.4
		After suction	37.5	12.5
		Increment	+5.3	5.0

the catheter sheath swabbed. Blood agar plates were inoculated with these swabs and were incubated at 37°C for 48 hours, when any organisms grown were identified.

Data were analysed using Student's *t*-test for paired data.

Results

Nine patients completed the study. Two patients were withdrawn because they developed clinically evident chest infections which required antibiotic therapy. There were no significant changes in the composition of the tracheal flora of the nine patients who completed the study.

Table 1 shows the results of total colony counts from air sampling. Values before and after suction are shown for both the conventional (open) and the Stericath (closed) methods on the first and second days. Each subject was sampled on three or four occasions with each method on both days. Table 1 also includes the incremental rise in colony counts associated with tracheal suction.

Table 2 compares more closely the average rise in colony counts before and after suction, using the air sampling technique. Both the conventional and the Stericath methods were associated with a significant increase in colony counts after suction. On average, 18.6 fewer colonies were grown when the Stericath was used ($p < 0.001$).

Table 3 shows the numbers of marker colony counts grown from settle plates after suction. No marker colonies

Table 2. Total colony counts measured by air sampling before and after tracheal suction using open or closed suction systems.

		Mean difference	SD	*t*-value
Open (conventional)	First day	+30.0	11.8	+7.61 ***
	Second day	+20.7	7.9	+7.82 ***
	Average	+25.3	7.7	+9.88 ***
Closed (Stericath)	First day	+8.1	5.1	+4.78 **
	Second day	+5.2	5.0	+3.19 *
	Average	+6.7	4.0	+5.1 ***
Difference	First day	−21.8	10.4	−6.29 ***
	Second day	−15.3	9.6	−4.79 **
	Average	−18.6	6.6	−8.36 ***

$p < 0.05$ * $p < 0.01$ ** $p < 0.001$ ***

Table 3. Marker colony counts measured on settle plates after tracheal suction by the open method.

	Distance	Mean	SD
First day	50 cm	13.5	5.4
	100 cm	1.4	1.1
Second day	50 cm	8.6	3.1
	100 cm	0.9	1.0

were grown before suction at 0.5, 1, 1.5 or 3 metres when either of the two suction methods was used. When the open method was employed, colonies were grown after suction at 0.5 metre (13.5 on day 1 and 8.6 on day 2) and at 1 metre (1.4 and 0.9), but no marker colony was grown at 1.5 or 3 metres on either day. No marker colony was grown on either day at any of the four distances when the Stericath was used.

Table 4 shows the comparison of the mean difference of settle plate colony numbers before and after suction. No colony grew when the Stericath was used, and thus this table serves as a comparison between the two suction methods.

Mixed flora containing the marker bacillus organisms from the subjects' sputum were obtained from the catheter sheaths of three of the nine patients. The method employed did not permit acccurate quantification of the number of colonies. Nevertheless, the growth of marker bacillus colonies derived from the sheaths was scanty compared with the growth from individual sputum samples on either day.

Discussion

The potential advantages of a closed system for tracheal suction over the conventional open suction technique include maintenance of ventilator parameters and reduction of contamination with potentially infectious organisms.

It is possible with the closed system to maintain the mode of ventilation without interruption during suction; inspired oxygen tension, positive end-expiratory pressure (PEEP)[6] and continuous positive airway pressure are substantially unchanged if catheters of an appropriate size relative to the tracheal tube are used.[7] Tracheal suction in a mechanically ventilated patient using the open method has been shown to be associated with a decrease in arterial

Table 4. Comparison of colony counts on settle plates before and after tracheal suction by the open or closed methods.

Distance		Mean difference	SD	*t*-value
50 cm	First day	+13.5	5.4	+7.48 ***
	Second day	+8.6	3.1	+8.43 ***
	Average	+11.0	4.1	+8.14 ***
100 cm	First day	+1.4	1.1	+3.84 **
	Second day	+0.9	1.0	+2.78 *
	Average	+1.2	1.0	+3.54 **

$p < 0.05$ * $p < 0.01$ ** $p < 0.001$ ***

oxygen saturation, cardiac arrhythmias and sudden death.[6,8] Closed system suction has been shown to be effective in preventing a decrease in arterial oxygenation, particularly in patients who require a high level of PEEP or who have a high alveolar-arterial oxygen tension gradient.[9,10]

Cross-infection in the ITU is a well recognised problem, with spread via the hands of staff considered to be an important route of transmission.[11] The bacteria involved have been shown to originate from a number of different sources including other patients and reusable respiratory equipment.[12] Staff use single-use, sterile catheters and wear disposable gloves for tracheal suction procedures in an effort to minimise the cross-infection risk.

This study showed that when an open suction system was used, environmental contamination occurred up to one metre away from the suction port, suggesting that the operator's clothes, the surrounding bed linen and the equipment become contaminated and may remain potential sources of infection for several hours or even days.[13] Cross-contamination is therefore almost unavoidable when an open suction system is used.

Opinions are divided concerning the importance of airborne contamination in the direct spread of organisms between patients. Our results appear to support the view that it is unlikely to be a problem, as no airborne organisms were detected 3 metres from the patient. Nevertheless, this route has been implicated in one hospital epidemic.[13]

The present study shows that there is significantly less environmental contamination when the Stericath is used. The results of air sampling reveal that there was a rise in the total number of nonspecific organisms detected after suction when either system was employed. This is to be expected, however, because the operator's own flora would have been shed into the investigation area as a result of the manoeuvres associated with undertaking a suction procedure. The increase in the postsuction colony count detected by the Reuter test when the Stericath was used ($+6.7$) was significantly lower ($p < 0.001$) than the increase associated with the open technique ($+25.3$). The settle plate tests, which could identify organisms which were known to colonise the patient's airways, failed to register any contamination from the patient when the Stericath was used, although these organisms were identified up to one metre away from the suction site with conventional open suction. This finding is consistent with the view that the Stericath effectively eliminates environmental contamination by organisms from the patient's respiratory tract. Much effort is directed at preventing the expulsion of contaminated gases from the exhaust ports of suction equipment[14] and ventilators as a means of preventing environmental contamination. We suggest that more attention should be paid to tracheal suction as a potential route for contamination.

Sheaths used for the protection of catheter devices represent potential reservoirs of infection in that organisms arising from the airway may contaminate the sheath and multiply there to act as a continuing source for re-infection each time the catheter is re-inserted into the patient. A previous study[5] which investigated catheter rather than sheath contamination showed no significant increase in risk to the patient over a 24-hour period. Billingsley and Radford (personal communication) have suggested that the tracheal tube represents a more likely site for bacterial recontamination of the airway than the suction catheters of either the closed or open systems. The present study appears to support this view. Only three of the nine catheter sheaths grew the marker bacillus, and in such low numbers that they were unlikely to have been of clinical significance. A further study is indicated to establish the influence of apparatus in contact with the airway as a site for sustaining viable organisms and a source for their re-inoculation into the host.

Every possible precaution should be taken to reduce the opportunity for cross-infection in very sick patients because they are all immune deficient to some extent. Although HIV has not been shown to be transmitted via tracheal secretions, less is known about the spread of opportunistic pneumonic pathogens. The Stericath system would probably be of benefit in patients colonised with multiresistant or highly infective organisms, where cross-infection between patients on ITU could produce disastrous results.

The potential risk to ITU staff who are subjected to environmental contamination with infective organisms for hours at a time deserves further consideration. The Control of Substances Hazardous to Health (COSHH) Regulations (1988) became fully effective on 1 January 1990. They affect *all* work where substances hazardous to health are handled or used. An employer is required by the Regulations to prevent exposure to micro-organisms which create a hazard to health, or to ensure that exposure is adequately controlled. Hospitals already spend substantial sums in providing for safe disposal of infected sharps and other clinical waste and in ensuring that equipment which has been used on an infected patient is decontaminated before it is serviced by technical staff. The Stericath is capable of eliminating aerosols of bronchial secretions contaminated with highly infective pathogens which would otherwise be generated during tracheal suction. Its use as part of routine ITU care must be an objective within the remit of the Regulations.

In conclusion, we have established the extent of environmental contamination which accompanies the use of the conventional, open tracheal suction technique in patients who are receiving IPPV from modern ITU ventilators. We have found the Stericath, a closed suction system, to offer an effective means of reducing environmental contamination from respiratory organisms. This device is considered to have benefits for both staff and patients, particularly with regard to highly infective organisms.

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SPECIAL ARTICLE

Mortality associated with anaesthesia

A case review study

K. GANNON

Summary

The review is based on an analysis of anonymous case record material at the Medical Protection Society's London Office for the 5-year period 1982–1986, in which death was associated with anaesthetic procedures. A total of 25 cases were analysed. The principal events which resulted in death were failed intubation, drug-related problems and problems with equipment. The principal contributory factors were inadequate supervision, inadequate pre-operative assessment and failure of communication. The present review suggests that supervision and training of junior staff, decision-making by senior staff and patterns of communication both within and between specialities are areas which should be selected for further research.

Key words

Complications; death.
Medicolegal.
Anaesthesia; audit.

The practice and delivery of medical care is being subjected to increasingly close scrutiny. Two major factors can be identified in this process. On the one hand there is growing public awareness of consumer rights in relation to medicine, and with this a concern both with safety and with redress when an accident occurs.[1] On the other hand there is a concern, both within and outside the profession, with standards of care; a concern which received added impetus with the publication of the recent White Paper 'Working for Patients'.[2] These factors are not, of course, completely independent but require somewhat different approaches to meet the particular concerns which lie behind them. Improvements in quality of care require a continuous process of monitoring and evaluation incorporating feedback, a process which has come to be known as audit and which has recently been the object of a great deal of attention.[3–5] The concern with accidents and with possible negligence requires an analysis of accidents and the factors which contribute to them. It has been pointed out recently that the systematic study of accidents in medicine has received a lower priority than studies of accidents in other areas, such as aviation.[6] This is despite the fact that there is evidence to suggest that medical accidents affect large numbers of people,[7,8] and have serious consequences both for the patients and staff involved.[9]

Anaesthesia is one area of medicine in which there has been a concerted attempt to investigate accidents in a systematic way. Many of the published studies in this area have employed the critical incident technique.[10–14] In most of these studies, human error emerged as a major contributory factor.

The topic of accidents in medicine has acquired a higher profile with recent changes in the insurance cover provided for hospital doctors against claims for negligence.[15] The fact that the financial burden for this has been transferred to the Health Authorities has led to concern being expressed about the possible negative consequences for the provision of health care.[16] These concerns have, by and large, centred around the potential impact on hospital services of large sums of money being awarded to plaintiffs and have led to suggestions about ways in which the risk of negligence actions might be reduced.[17] Such suggestions have focused on, for example, the need for more complete information to be given to patients about the risks of particular interventions. This ignores, however, the possibility that the number of claims might be decreased by reducing the numbers of deaths and poor outcomes which are due to avoidable factors. A useful first step in such a process is to analyse cases which have resulted in litigation, in an attempt to identify both the types of accidents that occur and any common avoidable factors involved in those accidents. The present report is based on a survey of claims against members of the Medical Protection Society (MPS) which originate from cases of death associated with anaes-

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thetic procedures. It follows on from a similar review of obstetric accidents.[18] It differs from the Confidential Enquiry into Perioperative Deaths (CEPOD) study of mortality associated with anaesthesia and surgery in that it is based on cases which have resulted in litigation.

The CEPOD study found that the overall death rate after anaesthesia was extremely low. However, the finding that human error is frequently a factor, both in cases of mortality and in near misses, suggests that this rate could be reduced even further if the causes of human error could be identified.

Method

Initially, a computer search of the MPS records was performed to retrieve all closed anaesthetic cases which involved the death of a patient and which were reported to the MPS over the 5-year period 1982–86. A total of 115 cases were found. Cases in which the following criteria were fulfilled were selected for further analysis:

(i) the MPS member was principally involved; (ii) expert opinion found evidence of negligence or substandard practice or avoidable errors; (iii) the death occurred in the UK or the Republic of Ireland.

This search yielded a total of 25 cases. The review itself was based upon anonymous material which gave details of the grade of the doctors involved, the nature of the procedure, whether it was elective or emergency, the age and sex of the patient and the written opinion of the MPS expert. This information was recorded on a form devised for the study.

Results

There were 11 male (average age 35.5 years) and 14 female patients (average age 42 years).

Table 1 shows the urgency of the procedure against the grade of the doctor principally concerned.

The five classified as emergencies involved the following procedures: a Caesarean section under general anaesthesia; a laparotomy for an acute abdomen; the institution of intermittent positive pressure ventilation for asthma; a suture of a perforated peptic ulcer; a laparotomy for a suspected perforated ulcer. Three of the anaesthetics were undertaken by registrars, one by senior house officer (SHO) and one by a doctor of unknown grade.

Events resulting in death

There were a number of common events which resulted in the death of a patient during anaesthetic procedures. These events are listed in Table 2.

The cases which involved failed intubation included several patients in whom difficulty might be expected for anatomical reasons; for example Hurler's syndrome (1) and patients who were obese or had short, thick necks (4). Three cases involved undetected oesophageal intubation and in a further two the tracheal tube apparently became displaced in the course of moving the patient.

The drug-related deaths could be divided into two types; the first type was associated with drug overdose (2) and the second involved a specific reaction to a particular drug (4). In both cases of drug overdose there were errors in the units of measurement. In one, the patient received ten times the dosage intended and in the other, one thousand times that intended. Two of the cases of a specific reaction to a drug involved the administration of beta adrenergic blockers to asthmatics, the third patient was given a combination of drugs which resulted in respiratory depression and acidosis and the fourth developed bronchospasm due to alcuronium sensitivity.

The equipment problems were due to incorrect assembly of the anaesthetic system (2), failure of the ventilator (1) and disconnection of the gas flow inlet (1).

The two cases of total spinal block occurred during the administration of epidural anaesthesia for obstetric procedures and both cases were further complicated by failed intubation. One of the patients had a previous history of difficult intubation and on this occasion two consultant anaesthetists failed to intubate when total spinal anaesthesia occurred. The second case involved an unsupervised junior who was providing a night-time epidural service on a split hospital site. In this instance, no anaesthetist was present when the total spinal occurred. In the absence of an anaesthetist, tracheal intubation was undertaken by a medical SHO on the cardiac arrest team, but it appears that the tube was misplaced.

The case which was considered to have represented a poor anaesthetic risk involved an elderly female patient with a bad medical history. It was the opinion of the expert that the particular procedure involved could have been carried out more safely under local anaesthesia.

The bilateral pneumothoraces occurred following the insertion of central venous catheters via the subclavian route. After insertion on the right side had failed, successful insertion on the left side was confirmed on X ray. However, the development of bilateral pneumothoraces was missed.

Contributory factors

The MPS experts were of the opinion that it was probable that most of these events would not in themselves have been sufficient to result in the death of the patient, had it

Table 1. Elective/emergency procedure by grade of doctor primarily involved in the 25 cases.

Grade	Emergency (*n*)	Elective (*n*)
Consultant	0	10
Senior registrar	0	1
Registrar	3	2
Senior house officer	1	5
General practitioner	0	2
Unknown	1	0

Table 2. Events resulting in death during anaesthetic procedures (25 cases).

Event	Number
Failed intubation	10
Drug related	6
Equipment problems	4
Total spinal block and failed intubation	2
Poor anaesthetic risk	1
Failure of monitoring in recovery units	1
Bilateral pneumothoraces	1

Table 3. Factors associated with anaesthetic mortality.

Factor	Number
Inadequate supervision	8
Inadequate pre-operative assessment (including inadequate history taking)	7
Failure of communication	5
Anaesthetist left patient	5
Unskilled resuscitation	3
Patient with dark skin pigmentation	3

not been for the presence of other associated factors. One or more of these factors were considered to be present in each of the cases and they are listed in Table 3.

Inadequate pre-operative assessment included some cases in which the patient was admitted on the day of the operation and was not seen by an anaesthetist and others in which the patient was premedicated before being seen by an anaesthetist. Poor history taking, such as failure to note asthma, was believed to be a factor in three cases. In five cases, the anaesthetist had left the patient. In one, he went over to tie the surgeons' gowns, during which time the patient was moved without his knowledge and the tracheal tube became displaced. There were three cases in which cyanosis was undetected because of dark skin pigmentation.

The experts considered that attempts at resuscitation were unskilled in three cases.

Inadequate supervision, which included allowing junior doctors to carry out, unsupervised, tasks at which they were not skilled, was thought to be a factor in eight cases. One of the cases of total spinal block, for example, involved a doctor who had only performed two epidurals before under supervision.

Poor communication operated in two ways. One was a failure of communication between medical specialities; for example, failure of the surgical team to notify anaesthetists of relevant aspects of the patient's history. The other was a failure of communication between doctors and nursing staff, such as failure to ensure that nurses in the intensive care unit (ICU) were fully informed of the need to monitor particular aspects of the patient's condition.

Discussion

Two caveats should be borne in mind when the cases presented in this review are considered. First of all, in most cases only one expert opinion was obtained, therefore there was a possibility of bias. Secondly, there are relatively few cases and they are a highly selected group, representing the worst possible outcome. Nevertheless, this sort of material provides a valuable starting point in an attempt to identify the incidents which result in anaesthetic mortality and, moving back a stage, the factors which contribute to this outcome. The best chance of reducing the number of cases with a poor outcome probably lies in the identification of these contributory factors. Each accident may be unique in itself, but is often the end result of a chain of events, components of which may be common to a range of accidents. For example, an unsupervised junior doctor who performs a procedure in which he has been inadequately trained may get into difficulty, but delays calling for help. Assistance may be slow to arrive and when it comes there may be further problems; for example, essential equipment may be faulty or missing. No single component in this sequence of events is necessarily problematic, but each represents an avoidable risk factor and when these factors are combined they increase the probability of a poor outcome. This point has also emerged from previous studies.[18–20]

The majority of deaths occurred during elective procedures, and only about one quarter of the patients were aged 60 years and above. Thus, neither age nor emergency were major factors in this series of deaths. This is different from the CEPOD finding, that the majority of deaths occurred in elderly patients and were often associated with progression of the presenting condition.

Again unlike some previous studies,[18] doctors of consultant grade were more frequently involved in these incidents. This may reflect factors specific to the reporting of cases in which litigation is involved or factors related to a small sample size.

Inadequate supervision emerged as a significant factor in these cases, as it has in a similar review of obstetric accidents[18] and in audits of mortality in anaesthetics[19] and surgery and anaesthetics combined.[20]

Criticisms were also made about inadequate pre-operative assessment. In several cases the patient was seen by an anaesthetist for the first time in the anaesthetic room. In some cases in which the patient was seen pre-operatively, the history-taking was poor, so that certain relevant aspects were not noted or their significance was not appreciated. There appear to be variations in practice with regard to the pre-operative assessment of patients by anaesthetists[20] and some disagreement about its importance.

In some instances the issue of history-taking was linked with a failure of communication between surgical and anaesthetic teams, in that anaesthetists were not informed about certain relevant aspects of the patient's history. The CEPOD report also drew attention to the issue of communication between the anaesthetist and surgeon. Communication problems may also occur between medical and nursing staff. Nurses may be unaware of the special requirements of certain patients after surgery; conversely, surgeons and anaesthetists may be unaware of deficiencies in ICU provisions.

Although failed intubation is an accepted hazard, the fact that misplacement of the tracheal tube can occur and fail to be detected, even by very experienced anaesthetists, suggests that it deserves further study on its own. In one case, three consultant anaesthetists failed to recognise that the tracheal tube was in the oesophagus.

Frequently, attention has been drawn to the fact that failed intubation, undiagnosed airway obstruction and unrecognised cyanosis are associated with patients with pigmented skin.[20,21] A similar finding emerged from the present review and underlines the need for special vigilance with such patients.

The case of death which occurred during the administration of epidural anaesthesia by an unsupervised junior anaesthetist working on a split site, emphasises a point made in a report on obstetric anaesthesia by the Association of Anaesthetists of Great Britain and Ireland.[22] The report states that 'potentially life threatening complications may occur at any time during an epidural block. It is essential that units offering an epidural service have an anaesthetist immediately available throughout the duration

of the block otherwise there could be avoidable delay in the initiation of resuscitation'. (It should be noted that this report appeared after the case described above).

A criticism frequently made by the experts was that the hospital notes were often inadequate or, on occasions, non existent. This not only made it difficult to give an opinion on a case, but would also have caused problems in the defence of a case in which there had been no evidence of negligence or avoidable error. This relates to the issue of inadequate history-taking, referred to previously. The Royal College of Surgeons of England has recently produced guidelines on medical records and notes. These recommend that the clinical record should contain both an initial history with details of previous illnesses and a full record of surgical and anaesthetic procedures, which includes details of pre-operative assessment and difficulties or complications encountered.[23]

The problems associated with history-taking, assessment of patients prior to anaesthesia and the discharge of patients suggest a need for standardised protocols to encompass these areas. In view of the increasing amount of day case work, which makes greater demands on junior doctors and paramedical staff, the use of standardized protocols would seem to be particularly important.

Many of the causes of death and the factors associated with them which emerged from this study were also identified in the CEPOD report. Factors such as lack of experience, inadequate supervision, drug effects and technical problems appeared in both series. This suggests that, at least in terms of the causes of death and avoidable factors associated with them, there may be relatively little difference between cases which come to litigation and those which do not. On the basis of the present data it is difficult to say precisely why certain cases come to litigation. It is possible that relatives may be more willing to sue if the patient was relatively young and the procedure was not an emergency, both of which features were applicable to the present series. Younger people undergoing elective procedures are not expected to die, therefore the unexpected nature of these deaths could be a factor in litigation. Another possible factor, albeit one which cannot be verified on the basis of the present data, might be the manner in which the death was explained by medical staff to the bereaved. There is a suggestion that people are more likely to sue if they believe some information is being withheld.[1]

There are also many similarities between the factors implicated in this study of anaesthetic mortality and those which have been found in critical incident studies. Currie, for example, identified near misses involving non-ventilation of the patient, disconnections, failed intubation and inadequate communication.[14] An earlier study[10] reported, amongst other incidents, near misses involving disconnections, extubations, and changes of position of airway devices. The same study also identified a range of factors associated with these, including poor communication, lack of training or experience, inadequate familiarity with surgical procedures and problems with supervision.

These similarities suggest that many of the specific errors and associated factors identified in critical incident studies can, if undetected, lead to the death of the patient. This reinforces the need for such studies and the necessity of acting on their findings. It also adds weight to the speculation of Cooper *et al.* that 'we suspect that the factors inducing error are similar regardless of final outcome'.[10]

It is worth considering why the same factors consistently emerge in series drawn from different populations with different selection criteria. Why should they continue to occur when they have been repeatedly identified and reported in the literature? A possible answer comes from consideration of one factor; that of training. In an early study employing the critical incident technique Cooper *et al.* commented: 'We are left with the impression that most of the errors and associated outcomes could be averted by a more structured approach to preparing residents for the environments into which they are often suddenly immersed'.[10] Problems with training and supervision continue to appear as factors associated both with near misses and deaths, and concerns about training and supervision continue to be expressed.[24–27] The Royal College of Surgeons has recently emphasized the need for consultants to participate fully in the training and supervision of juniors.[28] The evidence suggests that many of the lessons of these studies are not being learned. It may be that it is no longer sufficient simply to catalogue the errors and that more detailed research into some of the associated factors is required. For some time now 'Decision' theory has been applied to general clinical decision-making[29] and it may be relevant to apply this technique to an analysis of factors involved in accidents. The finding that anaesthetists of consultant grade were principally involved in many of the cases reported in this series suggests that decision-making by senior doctors might appropriately be studied in this way. For example, why do experienced anaesthetists reject the hypothesis that the tracheal tube is in the oesophagus and instead attempt to identify other problems, during which time the patient is becoming hypoxic? The issue of noncompliance by professionals[30] is a consideration which may be relevant here. This in turn raises the issue of standards of practice and their associated benefits. There is some evidence of a reduction in major preventable intraoperative injuries following the introduction of safety monitoring standards.[31] However, the benefits of such standards are not universally agreed. It has been argued that it is extremely difficult to relate a reduction in anaesthetic-related mortality unambiguously to the introduction of practice standards.[32] It has also been suggested that practice standards are frequently introduced before real benefits have been demonstrated and that the possible risks associated with monitoring are often ignored.[33] The question has been raised as to whether adherence to monitoring standards can compensate for poor judgement.[32] A more fine-grained analysis of particular factors may clarify the reasons for the occurrence of errors, suggest ways of reducing their frequency and assist in the selection of appropriate practice standards. Cooper *et al.*[10] have neatly expressed the logic of this approach: 'Decreasing the frequency of occurrence for the entire set of errors should decrease it for that subset with unfortunate outcomes'.

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Forum

Acid aspiration prophylaxis in morbidly obese patients: famotidine vs. ranitidine

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Summary

Famotidine and ranitidine were compared as agents for the prevention of acid aspiration syndrome in 32 morbidly obese patients undergoing vertical banded gastroplasty. Single-dose oral famotidine or double-dose oral ranitidine were administered on a random basis before surgery. Gastric contents were aspirated through a gastric tube, manually aided by the surgeon with the abdomen open. Mean (SD) gastric volumes were 13.8 ml (6.7) and 12.1 ml (13.0) for the famotidine and ranitidine groups, respectively. Mean (SD) gastric pH values were 6.2 (1.5) and 6.8 (1.5), respectively. There were no significant differences between the groups and no patient was considered 'at risk' (pH < 2.5 and gastric volume > 25 ml). We conclude that single-dose oral famotidine and double-dose oral ranitidine are equally effective for preventing acid aspiration syndrome in morbidly obese patients.

Key words

Gastrointestinal tract; stomach, pH, volume.
Histamine, H_2 antagonist; famotidine, ranitidine.
Complications; aspiration, morbid obesity.

Morbidly obese patients are prone to develop acid aspiration syndrome (AAS).[1,2] Factors that determine this increased risk are high residual gastric volume and acidity at the time of anaesthetic induction,[3] and a predisposition to regurgitate.[4]

Intravenous cimetidine[5] and intravenous[6] and oral[7] ranitidine have been shown to be effective in reducing gastric volume and increasing gastric pH in morbidly obese patients. Famotidine is a new histamine H_2-receptor antagonist which is more effective than cimetidine in reducing gastric volume and increasing gastric pH in healthy subjects[8] as well as in patients with hypersecretory digestive disease.[9] Famotidine is as effective as ranitidine in the prevention of AAS in nonobese patients undergoing either inpatient[10–12] or outpatient[13] elective surgery.

The purpose of this study was to compare the effects of oral famotidine and ranitidine, administered pre-operatively, on gastric volume and pH in morbidly obese patients.

Methods

Morbidly obese patients undergoing elective vertical banded gastroplasty were invited to participate in the study. Morbid obesity was defined as a body mass index (BMI) greater than 40 (BMI = weight (kg) height/sq m). Patients with gastrointestinal disease or those prescribed anticholinergics, opioids or H_2-receptor antagonists were excluded. Institutional approval and individual consents were obtained.

The patients were randomly allocated to two groups to receive one of the two study medications. The famotidine group received 40 mg orally the night before surgery, while the ranitidine group received 150 mg orally the night before and again 2h before surgery. All patients were premedicated with 15 mg of diazepam given orally the night before and 2h before surgery. All drugs were given with 20 ml of water. The patients fasted during the night and morning before surgery.

Anaesthesia consisted of pre-oxygenation for 3 min followed by rapid sequence induction with 5 mg of atracurium to reduce fasciculations, 6 mg/kg of thiopentone and 1.5 mg/kg of suxamethonium. Sellick's manoeuvre was performed and when the patient was apnoeic the trachea was intubated. Anaesthesia was maintained with 50% nitrous oxide in oxygen supplemented by halogenated anaesthetics or opioids.

When the abdominal cavity was open, a No. 18 French size Salem gastric tube was inserted into the stomach; its position was checked manually by the surgeon. The surgeon cross-clamped the pylorus, and gastric contents were then aspirated with a calibrated syringe. The surgeon completed gastric emptying manually while aspiration through the gastric tube continued. Gastric contents were measured with the syringe, and gastric pH was measured with a pH-meter (Corning digital 125, Halstead, U.K.). The duration of fasting was also recorded.

All data are presented as mean (SD). Comparisons between the two groups of patients for all variables, including demographic data and gastric measurements, were made with a two-sample *t*-test. A value of $p < 0.05$ was considered statistically significant.

Results

Thirty-two patients (25 female) were recruited to the study. The two groups were comparable for all demographic data

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Table 1. Demographic data.

	Famotidine	Ranitidine
Number of patients	16	16
Age; years	38 ± 6	36 ± 8
Sex; female/male	12/4	13/3
Weight; kg, mean (SD)	125 (21)	130 (18)
Height; cm, mean (SD)	160 (11)	163 (8)
BMI; kg/m, mean (SD)	48 (5)	49 (5)
Body surface area; m^2, mean (SD)	2.2 (0.2)	2.3 (0.2)

Table 2. Gastric volume, pH and duration of fasting for the two groups.

	Famotidine	Ranitidine
Number of patients	16	16
Volume of gastric fluid; ml, mean (SD)	13.8 (6.7)	12.1 (13.0)
pH of gastric fluid, mean (SD)	6.2 (1.5)*	6.8 (1.5)†
Fasting duration; min, mean (SD)	715 (47)	709 (44)

*Two patients in the famotidine group had no gastric aspirate.
†Three patients in the ranitidine group had no gastric aspirate.

(Table 1). Table 2 presents gastric measurements and fasting time. Five patients, two in the famotidine group and three in the ranitidine group, had no gastric secretions. There were no significant differences between the gastric volume and pH values of the two groups.

One patient in the famotidine group and two in the ranitidine group registered gastric volumes higher than 25 ml. All patients in both groups had gastric pH values greater than 2.5 and no patient was at risk of developing AAS according to the criteria suggested by Roberts and Shirley.[14]

Discussion

Acid aspiration syndrome continues to be a major cause of peri-operative mortality and morbidity[2,15] and morbid obesity has been associated with an increased risk of AAS.[4] At induction of anaesthesia 75% of obese patients remain 'at risk' according to the criteria of Roberts and Shirley.[3] Factors associated with morbid obesity related to AAS are the compression of the stomach by the abdominal mass, difficulty of airway management and, often, the presence of a hiatus hernia.

A gastric volume higher than 25 ml and a gastric pH lower than 2.5 have been considered as levels likely to result in aspiration pneumonitis;[14] but in a recent study on primates, Raidoo *et al.* suggested that a larger volume (0.8 ml/kg) at pH 1 would be necessary to consider a patient 'at risk'.[16] However, Raidoo's work, like that of Roberts and Shirley, was based on non-obese animal research, and extrapolation of these data to the morbidly obese patient would have to be done cautiously. Since the mean weight of our patients was 127.6 kg, the critical volume at pH 1, applying a value of 0.8 ml/kg, would be 102 ml. The unusually large size of this volume led us to apply, until more conclusive studies are available, the gastric volumes suggested by Roberts and Shirley.[14]

Therapeutic measures to reduce the effects of gastric content aspiration have centred on pre-operative administration of a histamine H_2-receptor antagonist. In nonobese patients, pre-operative oral or intravenous cimetidine[17] and ranitidine[18,19] administration effectively reduces gastric volume and acidity. These effects are similar in patients with morbid obesity.[5–7] Nevertheless, cimetidine, which has a short period of action and a variety of side effects, is not considered an ideal medication. Ranitidine is preferred for its greater potency, oral bioavailability, longer period of action and fewer side effects.

Famotidine is a new histamine H_2-receptor antagonist with antisecretory activity 30 to 100 times more potent than cimetidine and six to ten times more than ranitidine.[20] Its oral bioavailability varies from 37 to 45% and after oral administration its antisecretory effects last up to 12 h.[21] Side efffects, drug interactions, enzymatic induction and action on hepatic blood flow are all negligible in comparison with cimetidine and ranitidine.[20] Moreover, famotidine, like ranitidine, is superior to cimetidine for increasing gastric pH and is longer acting than ranitidine.[8,21] Gastric volume is reduced more fully with famotidine than with ranitidine.[10] Famotidine administered orally[11,12] and intravenously[10,13] has been used to premedicate non-obese patients for both inpatient[10–12] and outpatient[13] elective surgery.

The technique used to aspirate residual gastric fluid volume is critical for comparing results from different studies. Taylor *et al.*[22] found a mean difference of 14.7 ml between blind gastric aspiration and aspiration through a fibreoptic gastroscope. Hardy *et al.*,[23] on the other hand, demonstrated that aspiration controlled by the surgeon, as performed by our team, is trustworthy. To this method, we added clamping of the pylorus before gastric aspiration.

We found no difference between a single dose of famotidine and a double dose of ranitidine in respect of gastric volume and pH. Furthermore, although no patient in either group was at risk of developing AAS, one famotidine and two ranitidine patients showed volumes higher than 25 ml. Escolano *et al.*[10] found, in nonobese patients, that intravenous famotidine reduced gastric volume significantly more than did ranitidine. Our mean gastric volumes were slightly higher and mean gastric pH similar to those obtained in other studies for both the famotidine and ranitidine groups.[10,11] Abe *et al.*[12] obtained mean gastric volume and pH levels lower than ours in nonobese patients with oral famotidine. Dubin *et al.*,[13] in outpatients, reported a mean gastric volume somewhat higher and a mean pH lower in their single-dose famotidine group as compared to ours; both values were similar to ours for the double-dose ranitidine group. These differences may be attributable to pharmacokinetic changes of the H_2-receptor antagonists in morbidly obese patients, or to the different method of gastric content aspiration applied by our team.

We conclude that a single dose of famotidine and a double dose of ranitidine administered orally prior to surgery are equally effective in lowering the risk of AAS in morbidly obese patients.

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Diamorphine analgesia after Caesarean section

Comparison of intramuscular and epidural administration of four dose regimens

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Summary

In a randomised double-blind study, the efficacy, duration of action and side effects of five diamorphine analgesia regimens following Caesarean section are described. The time to next analgesia was shorter in the 5 mg intramuscular group (3.53 hours) than in any of the four epidural groups: 5 mg (5.7 hours, $p = 0.007$), 2.5 mg (4.76 hours, $p = 0.103$), 5 mg with adrenaline 1/200 000 (7.2 hours, $p = 0.001$) and 2.5 mg with adrenaline 1/200 000 (6.05 hours, $p = 0.007$). Multiple regression analysis showed that the addition of adrenaline significantly increased the duration of action of epidural diamorphine ($p < 0.05$). The 5 mg dose with adrenaline showed no advantage when compared with 2.5 mg with adrenaline ($p = 0.16$). No serious side effects were reported in any group.

Key words

Anaesthetic techniques, regional; epidural.
Analgesics; diamorphine.
Anaesthesia; obstetric.

Caesarean section under epidural anaesthesia has become an increasingly popular technique in recent years. Greater patient acceptability is combined with improved fetal condition at birth[1] and greater maternal safety.[2] Once the local anaesthetic block recedes, these patients experience pain for which powerful analgesics will be required. As the epidural catheter may easily be left *in situ*, these patients form one of the most suitable groups in whom epidural opioids may be used.

Since the first report of the administration of opioids into the epidural space was published in 1979,[3] there have been many studies in obstetric patients which have investigated different agents with respect to their efficacy, dose, duration of action and side effects.[4–9] The superiority of epidural over intramuscular administration in terms of duration and quality of analgesia has been demonstrated. However, the effect of opioid dose and the role of adrenaline is less clear.

The purpose of this study was to investigate the use of epidural diamorphine as an analgesic agent in patients following Caesarean section. We chose diamorphine because it has previously been shown to provide efficacious and prolonged analgesia,[5,6] while at the same time its pharmacokinetic profile would suggest a low risk of late respiratory depression.[10] Using a double-blind technique, epidural administration of two different doses of diamorphine, both with and without adrenaline, is compared to intramuscular administration.

Methods

Hospital ethics committee approval and informed consent from each patient was obtained. Both emergency and elective Caesarean section cases under epidural analgesia were included in the study. All patients were of ASA 1 or 2 status and had been delivered of a live singleton infant over 36 weeks' gestation. No patients received opioids at any stage during their labour or Caesarean section. Operative epidural blockade was achieved with 0.5% plain bupivicaine via a catheter placed at either L_{2-3} or L_{3-4} interspace. Peri-operative sensory block extended from T_4 to S_5 dermatomes.

After operation, each patient was randomly allocated to receive analgesia according to one of the five treatment regimens outlined in Table 1. In accordance with the double-blind design of the study, the drugs were prepared by an anaesthetist unconnected with the investigation. Two syringes were prepared, one for the epidural injection and the other for intramuscular use. One of these syringes contained normal saline. The study period commenced at the time that the local anaesthetic block was regressing and the patient first requested postoperative analgesia. The previously prepared epidural and intramuscular injections were then adminstered by one of the observer anaesthetists (I.D.S., K.E.K. or M.L.B.W.) who was unaware of their composition. Initial observations were made of pulse, blood pressure and respiratory rate, as well as pain and sedation scores on ungraduated 10 cm visual analogue scales; all patients received prior instruction in their use. In addition, patients were asked directly about nausea, vomiting and itching. These assessments were repeated at the following times: 15 and 30 minutes, 1, 2, 4, 8, 12, 18 and 24 hours. All observations were made by one of the specified observer anaesthetists (I.D.S., K.E.K. or M.L.B.W.).

The study period ended with the patient's next request for analgesia, when intramuscular papaveretum was administered. The total time since the previous administration was recorded as the time to next analgesia (TNA). All patients remained on the labour ward throughout the study

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Table 1. Postoperative analgesia regimens.

Group	Epidural	Intramuscular
1.	10 ml saline	5 mg diamorphine in 1 ml saline
2.	2.5 mg diamorphine with adrenaline 1/200 000 in 10 ml saline	1 ml saline
3.	5 mg diamorphine with adrenaline 1/200 000 in 10 ml saline	1 ml saline
4.	5 mg diamorphine in 10 ml saline	1 ml saline
5.	2.5 mg diamorphine in 10 ml saline	1 ml saline

period and for at least one hour after administration of papaveretum.

Statistical analysis

The Mann-Whitney U test was used to compare the duration of analgesia between groups. Comparison of the relative effects of intramuscular versus epidural administration, the role of adrenaline and of the two different doses of diamorphine was by a multiple regression technique with logarithmic transformation of time as the fitted variable (GLIM computer software). Chi-squared tests, with Yates' correction when appropriate, were used to compare linear analogue pain and sedation scores; a point more than 2.5 cm along the 10 cm scale was taken to indicate a significant score, 0 cm indicating no pain or sedation. Fisher exact tests were also used to compare the incidence of nausea and itching.

Results

One hundred and six patients were studied. Observations from 102 are included in the analysis. Three patients were lost from the study due to logistic difficulties in making the observations; the record chart of one patient was mislaid. The mean age and weight of patients in each group were comparable (Table 2).

Table 3 shows the mean time to next analgesia (TNA), its range, standard deviation and standard error of the mean for each group. The TNA was significantly longer in all the epidural groups when compared to the intramuscular group ($p < 0.01$) except for epidural diamorphine 2.5 mg, which, although longer, was not significant. There is a clear pattern between the epidural groups: the TNA was greater in both the adrenaline-containing and higher dose groups compared with their nonadrenaline and lower dose equivalents. However, the only epidural groups that showed a significant difference was between diamorphine 2.5 mg alone and diamorphine 5.0 mg with adrenaline ($p < 0.05$).

Multiple regression analysis showed a highly significant difference between the duration of analgesia of the intramuscular and epidural groups ($p < 0.001$). The addition of adrenaline to the epidural injectate also significantly improved the duration of analgesia ($p < 0.05$) but not in the 5 mg dose ($p = 0.16$).

Table 2. Mean (range) age and weight.

Group	n	Age; years	Weight; kg
1.	21	28.9 (18–39)	71.4 (48–98)
2.	22	29.9 (19–38)	65.8 (49–85)
3.	17	31.1 (23–41)	69.7 (50–95)
4.	22	30.4 (23–35)	70.4 (50–100)
5.	20	30.6 (18–39)	74.2 (50–105)

Table 3. Time to next analgesia (hours).

Group		n	Mean	Range	SD	SEM
1.	Intramuscular diamorphine 5 mg	21	3.53	1.2–15.7	3.37	0.74
2.	Epidural diamorphine 2.5 mg with adrenaline	22	6.05	1.5–24.0	4.78	1.02
3.	Epidural diamorphine 5.0 mg with adrenaline	17	7.20	1.6–26.5	5.59	1.36
4.	Epidural diamorphine 5.0 mg	22	5.70	1.75–13.3	3.43	0.73
5.	Epidural diamorphine 2.5 mg	20	4.76	1.0–12.5	3.35	0.75

The duration and quality of satisfactory analgesia for each group (defined as a pain score of less than 2.5 cm on a linear analogue scale) is shown graphically in Figure 1. All groups had improved analgesia within 15 minutes of administration ($p < 0.001$). At 4 hours, only the epidural 5 mg + adrenaline group still had improved analgesia to a $p < 0.01$ level when compared to its initial value. The quality of analgesia in the epidural groups was superior to the intramuscular group ($p < 0.05$) at 30 minutes; this was still the case at 2 hours (with the exception of the epidural 5 mg group) but at 4 hours there were no significant differences. Between epidural groups, significant differences were as follows: epidural diamorphine 5 mg + adrenaline was superior to diamorphine 2.5 mg alone at 1 and 4 hours and to diamorphine 5 mg at 1 hour ($p < 0.05$).

Figure 2 shows the level of sedation of each group plotted against time. There was an increase in all groups, but of less magnitude in the epidural with adrenaline groups. At 4 hours the epidural diamorphine 5 mg plus

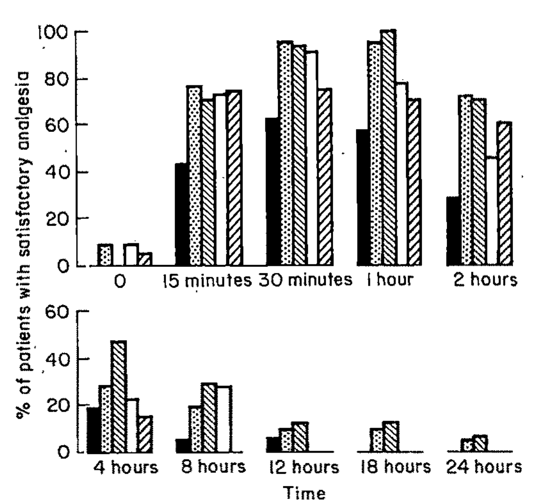

Fig. 1. Percentage of patients with satisfactory analgesia (linear analogue pain score < 2.5 cm). ■, intramuscular diamorphine 5 mg; ▤, epidural diamorphine 2.5 mg with adrenaline; ▨, epidural diamorphine 5 mg with adrenaline; □, epidural diamorphine 5 mg; ▧, epidural diamorphine 2.5 mg.

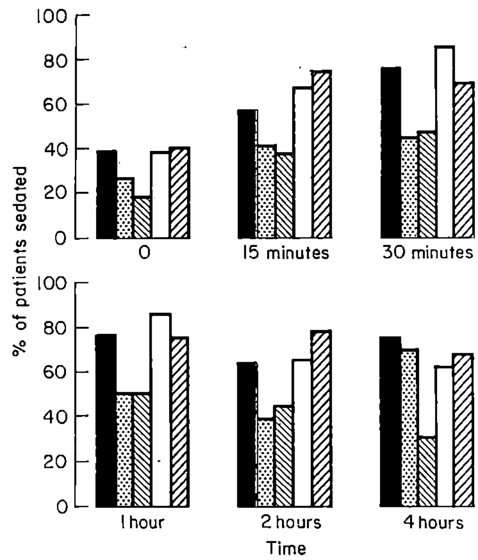

Fig. 2. Percentage of patients significantly sedated (linear analogue sedation score > 2.5 cm). See Figure 1 for explanation of bar graph markings

adrenaline group was significantly less sedated than all other groups ($p < 0.05$).

No significant respiratory depression was seen during the study period. The lowest respiratory rate recorded was 11 breaths per minute. This was in a sleeping patient, one hour after administration of epidural diamorphine 5 mg.

Table 4 shows the frequency of other side effects. Ten percent of patients in the intramuscular group experienced itching at some stage during the study period; the incidence in the epidural groups was 46% ($p < 0.01$). There were no significant differences between the epidural groups.

Although only one patient vomited, 27% were nauseous. No difference in the incidence of nausea between groups was demonstrated.

Table 4. Adverse effects.

Group	*n*	Nausea	Vomiting	Itching
1.	21	6	0	2
2.	22	6	0	10
3.	17	7	1	10
4.	22	2	0	7
5.	20	7	0	11

Discussion

Our study confirms that epidural administration of diamorphine to patients after Caesarean section provides a significantly better duration of analgesia compared to intramuscular administration. We have demonstrated that this duration of action is further increased by the addition of adrenaline. We did not find that administration of a larger 5 mg dose of diamorphine conferred any significant advantage over 2.5 mg.

In a study of similar design to our own, Macrae *et al.*[5] compared epidural diamorphine and epidural phenoperidine with intramuscular diamorphine. They found that the mean duration of action of 5 mg epidural diamorphine was 8.39 hours and intramuscular diamorphine 3.4 hours. Similarly, Semple *et al.*[6] reported that epidural diamorphine 5 mg lasted 9.87 hours, and if adrenaline 1/200 000 was added this increased to 12.51 hours. In contrast, our results of 5.7 hours with 5 mg epidural diamorphine and 7.2 hours when adrenaline is added are more modest, and more in keeping with those of Houlton *et al.*[4] who found that 5 mg epidural diamorphine lasted 6.3 hours. It is interesting to note that while Macrae and ourselves reported a comparatively large difference in the duration of action of epidural diamorphine 5 mg, we both found the duration of action of intramuscular diamorphine 5 mg to be very similar, 3.4 and 3.53 hours respectively. The reason for the epidural variation is unclear. One possible explanation might lie in the cultural differences of the populations studied; over 30% of our patients were from ethnic minority groups whereas both Macrae and Semple were studying a largely indigenous population in Dundee. Differences between cultural groups in their response to pain are well established.[11]

Concomitant administration of adrenaline with diamorphine causes local vasoconstriction within the epidural space, reducing blood flow and hence the rate at which systemic absorption takes place. The effect of adrenaline in significantly reducing plasma diamorphine blood levels after epidural administration has been demonstrated.[12] The postulated effect is to sustain a concentration gradient across the dura for a longer period of time, improve the overall proportion of diamorphine absorbed into spinal neural tissue and the overall duration of action. At the same time, lowered systemic levels may be associated with a reduction in side effects such as sedation. Semple *et al.*[6] in their study on the effect of adrenaline on epidural diamorphine, demonstrated an increased duration of action, but did not find it to be statistically significant. By utilising a multiple regression analysis technique we were able to isolate the relative effect of the addition of adrenaline, and in contrast to Semple, we demonstrated a significantly increased duration of action. Furthermore, we demonstrated the effect of adrenaline in significantly reducing the associated level of sedation.

Our results suggest that the 5 mg dose of diamorphine does not confer any advantage over 2.5 mg, either in respect of analgesic properties or in reduction of side effects. To our knowledge, all other studies investigating epidural diamorphine after Caesarean section have used 5 mg. In the absence of other published data it would be premature to draw too many conclusions from this finding, but on balance it would seem wise to recommend the lower dose as respiratory depression may be dose related.[13]

It is well known that there is a very large variation in the interindividual response to opioids. In all our groups the range of time to next analgesia was very wide, with at least one patient requesting further analgesia within 2 hours. Semple *et al.* suggested that the addition of adrenaline to epidural diamorphine increases its consistency in terms of analgesic effect. In our study, the standard deviation of the time to next analgesia was greatest in the adrenaline-containing groups: a finding which is inconsistent with this suggestion.

In keeping with previous work in similar groups of post Caesarean section patients,[5,6] we found no evidence of respiratory depression as judged by respiratory rate. However, rate alone may be a poor index of respiratory depression as was suggested by the work of Patrick *et al.*[14] Several risk factors are known to be associated with respiratory depression in patients receiving epidural opioids;[13] none of these, except the possibility of individual sensitivity, was present in this population. Nevertheless, patients who are given epidural diamorphine must always be carefully monitored; profound respiratory depression after epidural Caesarean section supplemented with fentanyl, a highly lipid soluble opioid like diamorphine, has been reported.[15]

The incidence of pruritus in the epidural groups was

similar to that in previous studies,[5,6] but in no patient was it troublesome enough to require any specific treatment.

In conclusion, we have confirmed that epidural administration of diamorphine is superior to intramuscular administration, that the addition of adrenaline improves its overall length of action and that a dose of 5 mg appears to confer no advantage over 2.5 mg. Of the dose regimens we studied, we conclude that epidural diamorphine 2.5 mg with adrenaline 1/200 000 provides the optimum choice for postoperative analgesia in this group of patients.

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Inhaled nebulised fentanyl for postoperative analgesia

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Summary

The effects of three concentrations of inhaled nebulised fentanyl citrate solution given for postoperative pain relief were studied. Each of 30 patients inhaled one dose of 3 ml of solution nebulised over 9 min. A combined analysis of pain relief, time to further analgesia and effect on respiratory frequency showed the highest concentration (318 μg/ml fentanyl base) to be more effective ($p < 0.01$) than the two lower concentrations (159 μg/ml and 64 μg/ml) which were indistinguishable from each other. There were no major side effects. This study provides evidence for the efficacy and safety of inhaled fentanyl for postoperative analgesia. Estimation of the delivered doses did not support the hypothesis that fentanyl is more effective by this route compared with other parenteral routes. Further studies are required to improve the method of delivery and investigate the pharmacodynamic features of this technique.

Key words

Analgesics; fentanyl.
Aerosols; analgesic administration.

Inhalation is a potentially useful alternative to the intravenous route for drug delivery. Chrubasik and colleagues[1,2] have examined the absorption pharmacokinetics and efficacy of nebulised morphine, and a single blind pilot study[3] has suggested that fentanyl might be suitable for inhalational administration. Both groups of investigators

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Table 1. Patient data, mass of fentanyl solution nebulised and operation type. Values are expressed as mean (SD).

	Fentanyl 64 μg/ml	Fentanyl 159 μg/ml	Fentanyl 318 μg/ml
Sex: m:f	3:7	1:9	1:9
Age; years	42.3 (14.6)	35.8 (7.2)	35.1 (11.9)
Weight; kg	66.9 (11.7)	64.7 (12.4)	62.4 (8.3)
Height; cm	167 (8)	154 (7)	160 (7) **
Mass nebulised; g	3.01 (0.31)	3.10 (0.23)	2.99 (0.42)
Operations (numbers)			
Laparoscopic sterilisation	1	3	7
Diagnostic laparoscopy	1	0	1
Abdominal hysterectomy	3	6	1
Vaginal hysterectomy	1	0	0
Orchidectomy	1	0	0
Inguinal herniorrhaphy	2	1	1
Laparotomy	1	0	0

**Statistically significant ($p < 0.01$).

suggested the intriguing possibility that the opioid concerned might be more effective when administered by the respiratory route than by conventional parenteral methods. The present study was designed to extend the work of the fentanyl pilot study in a double-blind fashion.

Method

The study, a double-blind comparison of three different concentrations of nebulised fentanyl citrate solution, was approved by the Hospital Ethics Committee. Patients gave informed written consent.

Patients with hepatic or renal disease, severe hypertension, symptomatic ischaemic heart disease, bronchial asthma or severe respiratory disease were excluded from the study. A history of allergy to opioids, or opioid addiction also led to exclusion. Patients, ASA 1 and 2, aged 20 to 68 years, undergoing one of a variety of elective general surgical or gynaecological procedures were recruited.

Patients who had given their informed consent and were potentially suitable subjects were premedicated with an oral benzodiazepine and received a routine balanced anaesthetic consisting of thiopentone or propofol for induction, nitrous oxide, oxygen and a volatile agent for maintenance and in most cases a muscle relaxant. All patients received intravenous morphine (range 2 to 13 mg) as part of the anaesthetic. Patients were admitted to the recovery room and when they were in pain and asked for their first dose of postoperative analgesia were entered into the study. They were randomised to receive a single dose (approximately 3 ml) of one of three concentrations of nebulised fentanyl citrate solution: 64 μg/ml, 159 μg/ml and 318 μg/ml fentanyl base (corresponding to concentrations of 100, 250 and 500 μg/ml fentanyl citrate). Only patients whose pain was sufficient to be treated with intramuscular opioid were included.

The solutions were delivered from Lifecare Micro-Neb disposable nebulisers attached directly to a facemask and driven by the hospital piped oxygen supply at 8 l/min for exactly 9 min. The nebulisers were charged with 5 ml of solution to avoid intermittent nebulisation and minimise evaporation effects.[4,5] Solutions were prepared by the hospital pharmacy from crystalline fentanyl citrate and sealed in ampoules labelled only with the group code. Immediately after use the nebuliser was sealed in a plastic bag to prevent further evaporation and weighed to determine the exact amount of solution expelled.

Patients described their pain before and 5 min after the end of nebulisation using linear visual analogue (LVA) pain scores (10 cm line marked at each end 'no pain' and 'agonising pain'). They also rated their analgesia as 'none' (0), 'a little' (1), 'moderate' (2), 'almost complete' (3) or 'complete' (4). The patients had been introduced to these scales on the previous day. If the patient judged analgesia to be inadequate 5 min after the end of nebulisation or at any time within the next 3 h, intravenous morphine was given until he or she was comfortable, and the time of administration recorded. Respiratory frequency, blood pressure and pulse rate were measured before and 5 min after nebulisation. The measurements were repeated and further assessments of pain and analgesia made at 15, 30, 45, 60 and at 30 min intervals to 3 h after the end of nebulisation or until the patient requested morphine. Arterial oxygen saturation was monitored continuously with a BTI BIOX III pulse oximeter. When not inhaling fentanyl, patients breathed 28% oxygen from a fixed percentage oxygen mask (Ventimask). Patients were questioned about subjective side effects before they left the recovery room.

Pain score change, time to further analgesia, and respiratory frequency change can be regarded as separate measurements of drug effect. In order to combine these various measures into one index of drug effect for each patient the variables were put on a common scale by ranking, and the arithmetic mean of each subject's three rank values used as a single combined index of relative drug effect. The groups were then compared using the Kruskal–Wallis and Mann–Whitney U tests on these averaged ranks to look for evidence of a dose response relationship. (Analgesia scores probably reflect the same information as pain score decreases and were not included in the calculation of average rank scores).

Statements of significance refer to the results of the Kruskal–Wallis test at $p < 0.05$ unless otherwise indicated.

Results

A total of 30 patients were recruited and provided three equal groups. There were no important differences between the groups in terms of gender, weight, age, amount of morphine given intraoperatively or mass of nebulised fentanyl solution delivered. The 159 μg/ml group were slightly shorter and the 64 μg/ml group slightly taller than the 381 μg/ml group ($p < 0.01$). The groups differed in the type of surgery undertaken (Table 1).

Pain scores ($p = 0.95$) and respiratory frequencies ($p = 0.62$) did not differ significantly between the groups before fentanyl administration (Tables 2 and 3). The groups differed significantly ($p < 0.05$) in pain score reduction 5 min after fentanyl inhalation, and in analgesia duration (Table 4) with the patients in the highest dose group (318 μg/ml) showing the greatest pain score reductions and

Table 2. Visual analogue pain scores before nebulisation and change by five min after nebulisation (maximum = 10).

		Fentanyl 64 μg/ml	Fentanyl 159 μg/ml	Fentanyl 318 μg/ml
Subject no.	1	7.5 (−4.5)	5.8 (−0.7)	6.9 (−5.4)
	2	6.4 (−3.3)	6.0 (−1.5)	7.7 (−2.0)
	3	2.9 (−2.1)	7.3 (0.0)	4.7 (−2.1)
	4	3.8 (−1.0)	8.2 (−1.3)	10.0 (0.0)
	5	8.9 (−2.7)	3.6 (−0.2)	5.0 (−4.0)
	6	8.2 (−0.8)	7.0 (+1.3)	10.0 (−2.4)
	7	8.9 (+0.2)	7.7 (−4.4)	6.4 (−3.7)
	8	5.3 (0.0)	8.2 (−1.5)	5.9 (−5.5)
	9	8.7 (+0.2)	7.3 (0.0)	7.2 (−5.4)
	10	3.9 (−3.0)	8.7 (+0.6)	6.1 (−3.6)
	Mean	6.5 (−1.7)	7.0 (−0.8)	7.0 (−3.4)

Table 3. Respiratory frequencies before nebulisation and change by 5 min after nebulisation.

		Fentanyl 64 μg/ml	Fentanyl 159 μg/ml	Fentanyl 318 μg/ml
Subject no.	1	12 (+1)	16 (+1)	16 (−4)
	2	26 (+2)	31 (−9)	18 (−8)
	3	22 (−2)	22 (0)	26 (−12)
	4	16 (0)	26 (−2)	24 (−4)
	5	16 (−6)	28 (−12)	16 (−4)
	6	24 (+2)	20 (0)	24 (−8)
	7	28 (−8)	14 (+2)	30 (−4)
	8	26 (−2)	24 (−4)	16 (0)
	9	20 (−2)	17 (−1)	26 (−6)
	10	13 (+3)	28 (−4)	16 (+2)
	Mean	20.3 (−1.2)	22.6 (−2.9)	21.2 (−4.8)

longest times to further analgesia. The 318 μg/ml group also had larger analgesia scores and greater decreases in respiratory frequency at 5 min than the other two groups but the differences between the groups on these latter two measurements were not statistically significant. Patients in the 159 μg/ml group tended to have longer times to further analgesic administration and greater decrease in respiratory frequency than those in the 64 μg/ml group, but smaller pain score decreases and lower analgesia scores. When the measurements were analysed together (see above) in terms of the average rank score the three groups differed significantly ($p = 0.002$). Paired comparisons of the average rank values (Mann–Whitney *U* test) showed no significant difference between the two lower dose groups ($p = 0.97$) but significant ($p < 0.002$) difference between the 159 μg/ml group and each of the other two groups. There was no clinically important respiratory depression (oxygen saturation < 90% or respiratory rate < 10). No patient became wheezy or complained of difficulty in breathing. Two patients had a slight dry cough intermittently during inhalation: one in the 64 μg/ml group (also coughing before aerosol therapy), and one in the 159 μg/ml group.

Eight patients complained of nausea after fentanyl (four in the 318 μg/ml group, two in the 64 μg/ml group, and two in the 159 μg/ml group). All except three of these (all in the 318 μg/ml group) had also been nauseated before fentanyl. Nobody complained of an unpleasant taste.

None of the groups showed a significant change in pulse rate or systolic blood pressure five minutes after fentanyl inhalation compared with immediately before ($p > 0.05$ Wilcoxon matched pairs).

Discussion

Patients receiving the highest fentanyl concentration (318 μg/ml) appeared to show greater evidence of opioid effect than those in the two lower dose groups when the degree and duration of analgesia and change in respiratory

Table 4. Times to escape analgesia in min.

		Fentanyl 64 μg/ml	Fentanyl 159 μg/ml	Fentanyl 318 μg/ml
Subject no.	1	80	*	90
	2	15	5	24
	3	5	5	80
	4	10	5	5
	5	5	12	*
	6	5	5	5
	7	5	120	10
	8	5	5	*
	9	5	5	30
	10	30	5	*

* No further analgesia within 180 min.

frequency were analysed together. The 159 μg/ml and 64 μg/ml groups were indistinguishable.

The preponderance of laparoscopies in the 318 μg/ml group was unfortunate since it weakens the argument for attributing the apparently better analgesia to the fentanyl. However, the pre-analgesia pain scores in all three groups were well matched and all patients had made a strong request for analgesia. Nine of the 14 laparoscopies requested further opioid analgesia within 3 h of receiving fentanyl, an argument against postlaparoscopy pain being so mild or fleeting as to explain the findings. There was also a trend to a greater decrease in respiratory frequency after fentanyl in the 318 μg/ml group.

In the three groups, doses of about 960 μg (318 μg/ml), 480 μg (159 μg/ml), and 190 μg (64 μg/ml) of fentanyl base were delivered from the nebuliser over 9 min. Clay and Clarke[6] estimate that about 25% of the dose released from a jet nebuliser will be deposited in the body, varying widely with experimental set-up and subject physiology. Of this 25%, 40 to 80% might be expected to deposit in the lungs, the rest being deposited in the mouth, nose, pharynx and upper airways.

Chrubasik and his colleagues found the average bioavailability of nebulised morphine in their experimental arrangement to be 17% of the amount placed in the nebuliser with wide intersubject variation.[1] They would probably have had residual drug left in the nebuliser at the end of useful nebulisation. Fentanyl is more lipid soluble than morphine which should lead to faster absorption from the deposited nebules but should have no marked effect on absolute bioavailability. Bioavailability of 20% in the present study would translate to intravenous equivalent doses for the three groups of approximately 190 μg, 95 μg and 40 μg of fentanyl given over 9 minutes; consistent with the clinical findings, only the highest dose showed enough effect to be distinguished. Worsley and his colleagues[3] apparently obtained effective analgesia with much lower doses of inhaled fentanyl; this allowed for evaporation effects and residual volume and their highest dose group probably represented between 200 and 250 μg emitted from the nebuliser over about 15 min. However, their pilot study was not investigator-blinded. About 75% of an intravenously-injected bolus of fentanyl is distributed to lung tissue at the end of the first pass of the bolus through the lung[7,8] and it is difficult to see why the pharmacodynamics of fentanyl absorbed from the lung should differ from those of intravenously injected drug.

This is undoubtedly an inefficient and awkward way to administer fentanyl. Constant supervision is required during delivery. Individual doses and the location of deposition will vary widely with respiratory pattern, even when other factors are as standardised as possible.[9] This particular regimen, therefore, could not be recommended for routine use. However it provides evidence for the safety and efficacy of the route and indicates that development of improved delivery techniques might well be worthwhile.

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Parents in the anaesthetic room

A questionnaire survey of parents' reactions

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Summary

One hundred and forty-one parents were asked to complete a questionnaire about their reactions after accompanying their child during induction of anaesthesia. Of 139 respondents, 99% believed that their presence was of benefit to their child, and 95% believed that they helped the anaesthetist. The degree of anxiety experienced by the parent did not significantly affect this view, nor was the degree of anxiety affected by the method of induction chosen by the anaesthetist.

Key words

Anaesthesia; paediatric, induction, parental presence.

Parental presence during induction of anaesthesia remains a controversial topic.[1] Anaesthetists and parents may have different opinions about the benefits of parental presence in the anaesthetic room, as has been clearly demonstrated in the correspondence generated by A. While's 'Personal View', published in the *British Medical Journal*.[2–6]

Most studies have examined the influence of parents on their child's behaviour during induction or the anaesthetist's reactions to the presence of parents at induction.[7–12] Conclusions both support and refute the belief that parental presence is beneficial.

The attitudes and opinions of parents who are present during the anaesthetic induction of their child is less well known. In the paediatric day surgical unit at Southampton it is usual to allow one parent into the anaesthetic room. In view of our current practice, and the relative paucity of information about parental opinion, we surveyed the reactions of parents who chose to be present at induction. We also wished to determine whether their experience was affected by the anaesthetist's choice of an intravenous or inhalation induction.

Methods

Hospital ethics approval for the study was obtained. Parents who had just accompanied their child during induction of anaesthesia were asked to fill in a questionnaire (see Appendix). No attempt was made to influence their wish to accompany their child, beyond the usual preoperative information given to parents. On leaving the anaesthetic room, consent was obtained and the parent was allowed to complete the questionnaire in their own time before leaving the theatre suite. Only parents of children aged 1 to 10 years, whose child was anaesthetised on an operating list attended by one of the authors were included in the study, which was carried out over a 2-month period.

Each parent was asked to grade his or her feelings whilst in the anaesthetic room and to decide whether their presence had been of benefit. They were also asked to describe any problems they observed and whether enough information had been given to them pre-operatively.

Results were analysed using the Chi-squared test where appropriate. Values of p less than 0.05 were considered to be statistically significant.

Results

One hundred and forty-one parents were invited to participate. Two parents declined. The results are therefore based on a total of 139 completed questionnaires.

One hundred and ten children (79.1%) were accompanied by their mother and twenty-nine (20.9%) by their father. Thirty-eight parents (27.3%) had been present at a previous anaesthetic induction. During the study period 31 children were unaccompanied by a parent.

Seventy-seven parents (55.4%) described themselves as calm, and 60 (43.2%) described themselves as anxious or very anxious. Two parents (1.4%) described themselves as terrified (Table 1).

One hundred and thirty-eight parents (99.3%) believed that their presence had helped their child, with 93% rating their presence as extremely or considerably helpful. One parent believed she was of no help to her child (Table 2).

One hundred and thirty-two parents (95%) felt they made the anaesthetist's job easier, 63% extremely or considerably (Table 3). Of the seven parents who felt they did

Table 1. Parents' emotional response.

Parents' response	Calm	Anxious	Very anxious	Terrified
Number (%)	77 (55.4%)	56 (40.3%)	4 (2.9%)	2 (1.4%)

Table 2. Parental help to child at induction.

Considerably or extremely	Moderately or slightly	Not at all
129 (92.8%)	9 (6.5%)	1 (0.7%)

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Table 3. Parental help to anaesthetist.

Considerably or extremely	Moderately or slightly	Not at all
87 (62.6%)	45 (32.4%)	7 (5%)

Table 4. Parental anxiety and previous experience.

Parents' reaction	Previous visit	First visit	
Anxious or very anxious	12/38 (31.6%)	50/101 (49.5%)	NS*

*NS: Difference not significant.

Table 5. Parents' response and method of induction.

Parents' response	Inhalation induction	Intravenous induction	
Anxious or very anxious	20/38 (52.6%)	48/99 (48.5%)	NS*

*NS: Difference not significant.

not help the anaesthetist, only one did not feel that she helped her child either.

Only four parents stated that they would not wish to be present during a future anaesthetic. Three of these felt they helped their child. The one parent who did not feel she had helped her child rated herself as terrified and did not feel she helped the anaesthetist.

Of those parents who described themselves as anxious, very anxious or terrified, 61 out of 62 (98.4%) believed that they were of some help to their child, with 90% regarding their presence as considerably or extremely helpful. All 77 (100%) of the calm parents believed that they were of some help. There was no statistical significance between these two groups.

Twelve out of 38 parents (31.6%) who had accompanied their child during a previous anaesthetic were anxious or very anxious, compared with 50 out of 101 parents (49.5%) present for the first time. There was no statistical difference between these two groups (Table 4).

Twenty out of 38 parents (52.6%) who witnessed an inhalation induction stated that they were anxious or very anxious, compared with 48 out of 99 parents (48.5%) who witnessed an intravenous induction. Two parents did not recall the method of induction. There was no statistical significance between these two groups (Table 5).

Seventeen parents (12.2%) felt that they had not been given enough information pre-operatively. Of these, the proportion of parents rating themselves as anxious or very anxious, seven out of 17 (41.1%), is not significantly different from the proportion rating themselves as calm, 10 out of 17 (58.8%).

Discussion

Allowing parents to accompany their child during induction of anaesthesia may reduce the effects of separation and alleviate the child's anxiety. The distressed child is at greater risk of laryngospasm or breathholding, and a turbulent induction may have potentially harmful long-term psychological effects.[7,13]

In this survey the overwhelming majority of parents who accompanied their child believed that they were of some help to their child (99%) or to the anaesthetist (95%). These results are similar to those of Smerling and colleagues[14] who found that a majority of parents believed their presence helped both the child and the anaesthetist. However, they also noted that parents rated the effect of their presence significantly higher than did the anaesthetist.

Despite almost half of parents describing themselves as anxious (43%) or terrified (2%), 97% would be prepared to accompany their child at a future anaesthetic, which confirms our own clinical experience. Again, these results are similar to those of Smerling[14] who found that while only 53% of parents described their experience as a pleasant one, 88% would wish to be present again. Schofield and White[11] found that 100% of parents present in the anaesthetic room believed they were helpful, and only 36% found their experience unpleasant or distressing.

In a pre-operative survey, Braude and colleagues[15] found that 50% of parents wished to be present at induction, citing their child's anxiety as the most common reason for their choice. One-third of parents would have changed their mind if the child was asleep following premedication. However, in the context of day case surgery heavy premedication is clearly undesirable. In contrast Hannallah and Rosales found that over 90% of parents wished to be present during induction.[8]

Despite the pre-operative information available, 12% of parents felt they had not been given enough information. Almost half of these parents described themselves as anxious, and the remainder as calm. Although fewer parents who had been present at a previous anaesthetic described themselves as anxious compared with those attending for the first time, the difference between the two groups was not significant. It is not clear therefore that additional information at the pre-operative visit, as advocated by several authors,[8,11,16] would reduce the level of anxiety experienced by parents.

In this study the degree of anxiety experienced by parents did not affect their belief that they were helpful. However, we made no formal attempt to determine whether parental presence or anxiety influenced the quality of induction. In our hospital a randomised, controlled trial in which some parents are precluded from being present while others are encouraged is probably unethical. Several studies do shed light on this problem. Hannallah and Rosales[8] found that parental support for preschool children resulted in a significant reduction in the number of upset children, despite 24% of parents judged to be anxious. As noted above, Smerling *et al.*[14] found that although half of parents rated themselves as anxious, the majority were felt to have been helpful by the anaesthetists involved. Hickmott and colleagues[10] were only able to demonstrate an increase in the time taken for induction by 48 seconds when mothers were present. No difference was found in the quality of induction.

In contrast Schofield and White[11] found that 7% of parents were judged to have been unhelpful by the anaesthetists, yet all parents believed themselves to be helpful. Bevan and colleagues[9] found that highly anxious parents adversely affected their child's behaviour, both at induction and one week postoperatively. They concluded that pre-operative assessment of parental anxiety might be useful to exclude highly anxious parents from the anaesthetic room. We have found that the degree of anxiety experienced by parents made no difference to their perception of their contribution. It may therefore be difficult to persuade anxious parents that their absence would benefit their child, whilst encouraging other parents to be present in the anaesthetic room.

We were unable to demonstrate an association between the method of induction and the degree of parental anxiety experienced. It is reassuring to know that an intravenous or inhalation induction seems equally acceptable to parents.

The main findings of the present study are that the majority of parents regard their presence during the anaesthetic induction of their child as helpful to that child, and that the degree of parental anxiety does not significantly affect this view. Whether individual anaesthetists believe that the presence of a parent affects the quality of induction will no doubt continue to be a matter for debate. We believe that our findings, and the results of other studies showing a beneficial effect of parental presence with a low incidence of problems, support our belief that where possible, parents should be allowed to accompany their child into the anaesthetic room.

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Appendix

Questionnaire

1. Is this the first time you have accompanied your child during an anaesthetic? Yes No
2. If your child needed another anaesthetic would you choose to be present? Yes No
3. How would you describe your feelings in the anaesthetic room? Calm Anxious Very Anxious Terrified
4. Do you think your presence helped your child? Not at all Slightly Moderately Considerably Extremely
5. Do you think your presence made the anaesthetist's job easier? Not at all Slightly Moderately Considerably Extremely
6. Did you notice any problems in the anaesthetic room? Yes No
7. Had you been given enough information about what to expect when your child went to sleep? Yes No
8. Was your child anaesthetised with an injection or a mask?
9. Did you feel unwell? If yes: dizzy/faint/other . . .
10. In your opinion should parents be encouraged or discouraged from being present?
11. Other comments . . .

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Sensitivity to curare in patients with upper and lower motor neurone dysfunction

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Summary

Sensitivity to the action of nondepolarising relaxants was compared in muscles of upper and lower limbs in four syringomyelic patients undergoing elective neurosurgical procedures. It was observed that muscles with signs of lower motor neurone dysfunction are supersensitive to the action of nondepolarising relaxants. Terminal sprouting of motor axons and the occurrence of newly formed neuromuscular junctions may be responsible for a low synaptic efficacy and may explain the high sensitivity to factors that reduce the safety margin of neuromuscular transmission.

Key words

Neuromuscular relaxants; syringomyelia.

Syringomyelia is a pathological condition in which motor deficit of the upper limbs may be frequently caused by lower motor neurone dysfunction and lower limb deficit by a pyramidal lesion. Resistance of centrally denervated muscles to the action of nondepolarising relaxants is well documented.[1–9] However, little is known about the sensitivity of denervated muscles in patients with lower motor neurone dysfunction.[1]

Experimental evidence demonstrates that extrajunctional acetylcholine receptors appearing after denervation may have a poor affinity for tubocurarine,[10,11] which, it has also been shown, may exert an agonist type of action on denervated muscles in some animals.[12] Clinical experience, on the other hand, indicates that sensitivity to curare might be greater than normal in patients with lower motor neurone dysfunction. Decremental responses and increased jitter, in fact, are common in electromyographic examinations of these patients.[13–18]

We report clinical observations which indicate that denervated muscles of syringomyelic patients have an increased sensitivity to the action of nondepolarising relaxants.

Methods

Patients were scheduled for elective neurosurgery. They were premedicated with diazepam and atropine. Anaesthesia was induced with fentanyl and thiopentone and maintained with either halothane or isoflurane, nitrous oxide and oxygen. Ventilation of the lungs was adjusted to produce a normal end-tidal carbon dioxide concentration, and the heart rate was recorded with an ECG monitor.

Neuromuscular block produced by the intubating dose of nondepolarising relaxants was assessed by the use of a Datex Relaxograph and at various intervals, a Medelec 'MS 92a' unit was used to compare the extent of neuromuscular blockade in different muscles. Motor nerves were stimulated at 2 Hz with supramaximal stimuli given in trains-of-four or in trains-of-nine. The extent of block was assessed by the evaluation of fade. Fade was given by $(1-T4/T1) \times 100$; where T4 is the amplitude of the fourth response in a train and T1 is the amplitude of the first response.

To increase the reliability of the procedure, studies that had been initiated with the Datex unit were completed with the Medelec and vice versa. The same surface electrodes were used in both examinations.

Case histories

Patient 1, a 74 kg, 45-year-old woman was admitted to hospital with a history of many years of cervical pain and progressive weakness of the left upper limb.

The neurological signs were hypoaesthesia, hypotonia, muscular atrophy, weakness and absence of tendon reflexes in the upper limbs. She had paresis of the lower limbs with brisk reflexes and extensor plantar responses, and impaired sensation in the upper trunk. The magnetic resonance study showed a syrinx from C_1 to D_7 and a Chiari malformation.

The fade caused by the intubating dose of vecuronium (0.08 mg/kg) was monitored with the Datex on the left adductor pollicis brevis; comparisons with fade demonstrated by the Medelec unit on the left flexor hallucis brevis were performed at the times indicated in Figure 1. Fade was greater on the denervated limb.

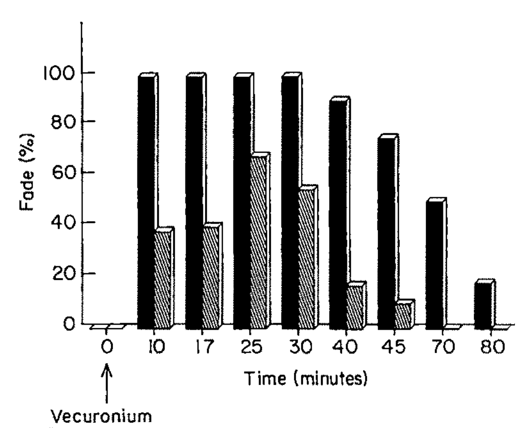

Fig. 1. Patient 1, ■, hyporeflexia in left arm; ▨, hyperreflexia in left leg.

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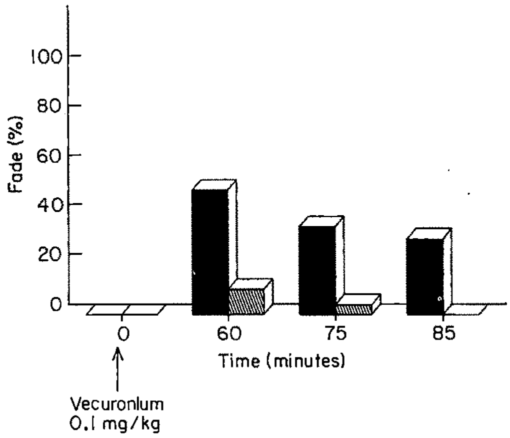

Fig. 2. Patient 2, ■, hyporeflexia in right arm; ▧, hyperreflexia in right leg.

Patient 2, a 65 kg, 21-year-old woman was admitted to hospital with a one-year history of gait disturbances and upper right limb weakness.

The neurological signs were of mild impairment of right lower cranial nerves, weakness, atrophy and sensory loss of the right upper limb, hyporeflexia in both upper limbs, spastic paraparesis, and cerebellar ataxia.

A magnetic resonance study demonstrated a syrinx from the foramen magnum to D_{11}, craniocervical junction malformation, and a Chiari malformation. Fade caused by the intubating dose of vecuronium (0.1 mg/kg) was monitored with the Datex on the first dorsal interosseous of the right hand; comparisons with fade demonstrated by the Medelec unit on the right flexor hallucis brevis were performed at the times indicated in Figure 2. The fade was seen to be greater on the denervated limb.

Patient 3, a 74 kg, 25-year-old man was admitted to hospital with a 6-month history of progressive weakness and atrophy of the right upper limb. He had weakness, atrophy and hyporeflexia of all right upper limb muscles which was worse in the hand. He had brisk reflexes in the lower limbs, and no sensory impairment. Magnetic resonance showed a syrinx from C_2 to D_{10}.

Fade caused by the intubating dose of pancuronium (0.07 mg/kg) was monitored with the Datex on the right adductor pollicis brevis, and compared with the fade demonstrated by the Medelec unit on the same muscle of the left hand performed at the times indicated in Figure 3.

The fade was greater on the denervated arm. Twenty-five minutes after induction of anaesthesia the Medelec unit revealed a fade of 82% and 95%, respectively, in the left and right trapezius muscles (not shown in figure).

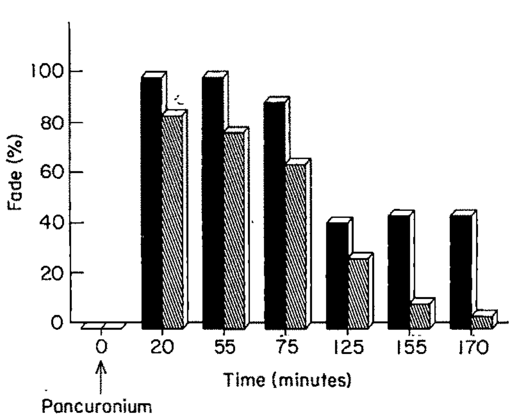

Fig. 3. Patient 3, ■, hyporeflexia in right arm; ▧, normal left arm.

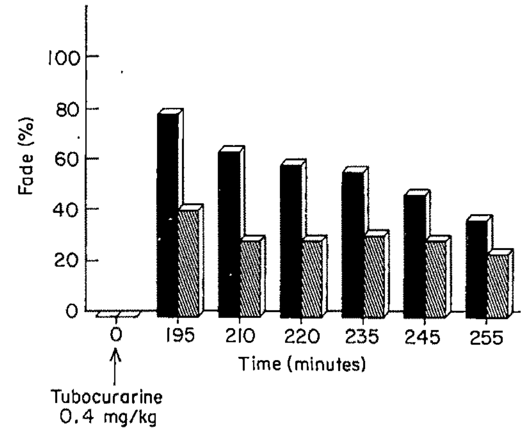

Fig. 4. Patient 4, ■, hyporeflexia in right arm; ▧, hyperreflexia in left arm.

Patient 4, a 57 kg, 40-year-old woman was admitted to hospital with a history of left hemiparesis at birth and an 8-year history of gait disturbances and progressive weakness and impairment of sensation at the right upper limb. She had severe weakness and muscular atrophy (distally more than proximally) of the right upper limb with complete absence of tendon reflexes, mild hyperreflexia of the left upper limb, muscle atrophy of the left lower limb, and brisk reflexes and extensor plantar responses at the lower limbs.

There was a syrinx from C_2 to D_7 and hydrocephalus. The fade caused by the intubating dose of tubocurarine (0.4 mg/kg) was monitored with the Datex in the left adductor pollicis brevis. Comparisons with fade demonstrated by the Medelec unit on the same muscle of the right hand were performed at the times indicated in Figure 4. There was prolonged curarization in both muscles and a greater fade was present on the right (denervated) muscle.

Discussion

Our results indicate that lower motor neurone dysfunction may be followed by increased sensitivity to the action of non-depolarising relaxants. Proliferation of extrajunctional receptors has been proposed as one of the possible mechanisms of the resistance to curare exhibited by centrally denervated muscles.[1–9] The same mechanism may have been present in the denervated muscles of our patients.

Since proliferation of extrajunctional receptors is a typical consequence of lower motor neurone dysfunction,[19] the extent of the proliferation may be much greater in muscles with increased sensitivity to curare than in muscles with reduced sensitivity.[20–21] A correlation between the degree of terminal sprouting of the motor nerve and the density of extrajunctional receptors has been observed in experimental animals after presynaptic blockade of neuromuscular transmission.[22] It has also been observed that the synaptic strength of newly formed neuromuscular junctions is poor[15,23,24] and seems to be inversely proportional to experimentally altered motor unit size.[25]

We think, therefore, that the presence of less effective synapses was the most important factor contributing to the supersensitivity to curare observed in our patients.

It should be considered, however, that the safety margin of neuromuscular transmission may be greatly increased by contralateral denervation.[26] We wonder whether the same phenomenon could be responsible for the resistance to curare appearing after decentralisation.

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Correspondence

On demand epidural fenatanyl

We were interested to read the report by Drs Welchew and Breen on patient-controlled on-demand epidural fentanyl (*Anaesthesia* 1991; **46:** 438–41). We feel, however, that their conclusion that this study demonstrates a clear increase in the potency-duration of epidural fentanyl over the intravenous route may be overstated. Whilst we agree that they have shown that the intravenous group received statistically more fentanyl than epidurally, this could well be a function of the analgesic prescription. If the 20 μg/hour background infusion is subtracted from the mean hourly

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dose rates, respective bolus doses of 5 μg and 20 μg for epidural and intravenous administrations would show that patients actually demanded analgesia more frequently in the epidural group. We have shown that with intravenous PCA, patients with similar pain and sedation scores demanded analgesia at rates independent of bolus size.[1] Dr Welchew's study has demonstrated that epidural fentanyl with 5 μg boluses has equivalent analgesia to intravenous PCA with 20 μg bolus size. An alternative conclusion is that these authors were comparing intravenous PCA using two bolus sizes. In order to validate the authors' statement that epidural fentanyl has a potency duration of 2.2, the epidural and intravenous bolus sizes need to be equivalent. If this results in fewer demands together with a lower plasma fentanyl concentration (measured via a central venous sampling catheter) then the authors statements regarding epidural versus systemic administration could be validated. This paper unfortunately fails to address these important points.

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Reference

1. OWEN H, KLUGER MT, PLUMMER JL. Variables of patient-controlled analgesia 4: the relevance of bolus dose size to supplement a background infusion. *Anaesthesia* 1990; **45:** 619–22.

We read with interest the paper by Drs Welchew and Breen on patient controlled on-demand fentanyl which compared the effects to the drug given intravenously and epidurally. (*Anaesthesia* 1991; 46:438–41). There was a fourfold difference in the dose of fentanyl delivered per demand to the intravenous group (20 μg) as compared to the epidural group (5 μg). This would naturally bias the outcome of the study towards the intravenous group receiving a cumulatively greater dose, a result which was indeed found.

More interestingly, if one considers the average number of successful demands per hour rather than the total dosages, there is a case to infer the opposite conclusion than the authors intended. Based on Table 2, which shows the mean rate of fentanyl consumption in the two groups, the average number of successful demands for the epidural group is nine and for the intravenous group only five. This is further corroborated by evidence from Figure 5 which compares the mean hourly consumption for the two groups. Four hours after the loading dose, the mean number of demands per hour calculated graphically is 8.5 for the epidural and 4 to 5.5 for the intravenous group. In both cases the number of demands are much less for the intravenous group. Unless the dose ratio utilized is based on a standard study concluding that a 4:1 ratio of intravenous to epidural fentanyl was equi-analgesic, the case could be made that intravenous fentanyl is more effective in providing postoperative pain relief. These anomalies would not a· :e if both groups had received the same dose of fentanyl per demand. Also of note is the fact that if the intravenous group were to receive the maximum allowed infusion in the first hour for pain relief, each patient would get a total of 11.16 μg/kg/hour. This is based on the loading dose, background infusion and on a demand dose of 20 μg with a lockout interval of 2 min. Dosages above 3 μg/kg are known to decrease both tidal volume and respiratory rate.

In a scientific study, the authors are of course entitled to use those dosages in a supervised environment. Although it is well documented that patient controlled analgesia is associated with underutilisation of the allowed dosages, these values should not be recommended for routine use.

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A reply

Thank you for giving us the opportunity to reply to Drs Kluger and Owen's letter. They criticise the fact that two different doses of fentanyl were given via the two different routes. In the first of their series of papers on PCA,[1] they concluded that there is such a thing as an optimum bolus size for PCA. We have considerable clinical experience of using fentanyl epidurally and intravenously by PCA. This has shown us that an epidural bolus of much more than 5 μg would lead to excessive sleepiness, whilst an intravenous bolus of much less than 20 μg would lead to inadequate analgesia. Our trial had no dropouts due to inadequate analgesia or excessive opioid effects, and the pain scores were exceptionally good. This compares with dropout rates of 13/21,[1] 2/19,[2] 28/37,[3] and 7/45[4] in Dr Owen's series.

Dr Owen's own paper[4] is central to his criticism of our work. Figures 1 and 2 of this paper clearly show that the demand patterns, cumulative morphine consumptions and total morphine consumptions in the patients having 0.7 mg and 1.0 mg bolus doses, were almost identical. On the other hand, the group having bolus doses of 0.4 mg had a much lower consumption pattern, leading to a lower total morphine dose consumed. In the middle of their discussion they explain 'that this phenomenon could be a result of a suboptimal PCA prescription'. It should be obvious that when the PCA bolus dose is progressively reduced, patients will eventually be unable to maintain adequate analgesia. It should come as no surprise that progressively decreasing bolus size below a critical threshold would lead to a progressive decrease in the total amount of analgesic consumed. This explanation would fit their data better and is the exact opposite of their conclusion. The good quality pain scores in our patients would suggest that none of them had a 'suboptimal PCA prescription'.

In the series of four papers,[1–4] a total of 15 regimens were compared, yet despite obviously inadequate analgesia in many of the patients, leading to their withdrawal from the trials, not once was a statistically significant difference in pain scores between groups shown. The numbers of patients required in each of these trials was calculated using the variability in PCA demand data not the variability in the pain data. As they always used the relatively insensitive PAIN AUC method of measuring pain, none of their trials had the power to resolve even large differences in pain scores. As it was a central tenet in these papers, and specifically the last one,[4] that there was no difference in the amount of pain suffered by patients in the different groups, the lack of a statistically significant difference in pain scores between the groups was obviously not relevant. Once the pain measurements are shown to be invalid, the conclusions also become invalidated and cannot be used to criticise other work.

To extrapolate from a paper on morphine given intravenously to women having gynaecological surgery, to our paper on men and women having epidural and intravenous fentanyl for upper abdominal surgery would have been an adventurous move even if based upon good

evidence. The paper by Owen, Kluger and Plummer[4] does not form an adequate basis for this.

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A reply

Thank you for the opportunity to reply to the letter from Drs Ali, Digger and Perks. These authors have raised several issues which I would like to address separately. Firstly, they have completely ignored the directly-measured pain scores which show that both groups of patients had excellent pain relief, with generally well matched pain scores, although there were small but statistically significant advantages for the epidural group. These authors have not attempted to explain how the epidural group could consume less than half as much analgesic as the intravenous group, yet have slightly better pain relief.

The second issue which this group raise is their use of the demand rate from the PCA machine as a measure of pain. This would mean that long acting drugs given by PCA, which generate fewer demands in unit time than shorter acting drugs, would therefore give better pain relief. There is no evidence to support this and it goes completely against the concept of using PCA as a way of comparing drugs. These authors appear to think that the inferred pain data generated in this way are more relevant than the directly measured pain scores actually published, which they ignored. The third, and arguably biggest, problem with this group's letter is that they have made a fundamental mistake with their arithmetic. They have included the 20 μg/hour background infusion of fentanyl in their calculations of demand rates. When this is removed, the actual demand rates taken from Table 2 are 5 per hour in the epidural group and 4 per hour in the intravenous group. This difference is not statistically significant and merely demonstrates how closely matched the two regimens were.

Finally, the authors of this letter have taken the figures from a standard textbook on anaesthesia which tells us that a bolus of 3 μg/kg of fentanyl will decrease respiratory rate and tidal volume and compared it with the possible maximum dose obtainable from the PCA machine in an hour. Firstly, the bolus size was less than 0.3 μg/kg and it is quite wrong to compare the textbook figure for a bolus with a calculated hourly dose. Secondly, the maximum dose actually given to any patient in this trial was 4 μg/kg but given over an hour. Thirdly, residual pain is analeptic and antagonises the sedative and respiratory depressant effects of opioids. Patients with severe postoperative pain, immediately after major surgery will need large doses of opioids to reduce their residual pain to acceptable levels. Under these circumstances, as long as there is still some residual pain, the respiratory depressant effects of the opioids are minimal, while CO_2 excretion and oxygenation are improved by losing the restrictions imposed by severe pain. It has long been recognised that patients using PCA systems very rarely give themselves complete pain relief, and the pain scores in our trial demonstrate that they did indeed leave themselves with some small amounts of residual pain.

All patients having opioids should have sensible prescriptions which make some allowance for the huge variability in their requirements and the patients themselves should be monitored carefully. Having said that, I can see little point in taking information out of context and then trying to apply it rigidly everywhere. As Drs Savarese and Lowenstein put it in their editorial,[1] there is 'no anaesthesia by cookbook'.

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Intubation through the laryngeal mask

I am concerned by the paper from Heath and Allagain (*Anaesthesia* 1991; **46:** 545–8), as some of the suppositions and suggestions they make are not backed up by or based on their research. In the first instance, they did not apply the technique to patients with unexpected difficult intubation, but to 100 patients presenting for routine surgery, of which only three had previously been noted to be difficult although we are not told how difficult, or by whom these previous intubations had been performed. They state that the laryngeal mask (LM) can almost always be placed satisfactorily and I would agree that this is true for patients with normal anatomy. Brain suggests that the LM may be easier to insert in patients with an apparently anterior larynx,[1] but this suggestion has not been formally tested. There are several reports of successful placement of the LM following failed intubation,[2–4] but without a proper study, ease of LM placement in these circumstances cannot be inferred.

They also state that the aim of prediction is to allow appropriate preparations to be made and sophisticated techniques such as fibreoptic intubation to be employed. Whilst I would agree that making appropriate preparations is important I would suggest that the main aim of prediction is to allow a safe (not necessarily sophisticated) technique, such as inhalational induction followed by direct laryngoscopy or possibly awake intubation. Safety, and not sophistication, must be our primary concern.

I agree that it is reasonable to practise the technique described on elective cases, in patients with caps and crowns and maybe patients anticipated to be difficult, providing preparations for dealing with failure are made. Their third indication (that they admit is controversial) is unexpected difficulty in patients at risk of regurgitation. Without releasing cricoid pressure the success rate in their study was 56%. Presumably some of the failures resulted in oesophageal intubation which is on occasion notoriously

difficult to recognise, particularly in the pre-oxygenated patient. An unrecognised blind oesophageal intubation is surely in most instances more dangerous than a known failed tracheal intubation. The old adage is well worth repeating that patients do not die from failure to intubate but from failure to oxygenate.

One point raised by the authors with which I can wholeheartedly agree is that anaesthetists faced with a difficult or failed intubation, in a patient not at risk of aspiration, should try the technique described, being sure to report failures as well as successes; reporting bias can be an enemy of such correspondence.

I should say that I am firmly in favour of developing and practising techniques to aid intubation (gum elastic bougie, blind-nasal intubation fibreoptic intubation and indeed the new method described by the authors of the paper concerned), but I feel that until the value of the method is established in cases of difficult or failed intubation, it should not be recommended for use in these circumstances particularly in patients at risk of regurgitation as part of a failed intubation drill.

So far, all the authors have described is a technique for tracheal intubation of routine cases that is less successful than the established method using a Macintosh laryngoscope.

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A reply

The negative response of Dr Frerk is disappointing. We feel that all of his legitimate concerns were adequately, if briefly, discussed in our paper. Perhaps what he really objects to is the title. We might have tried 'Intubation through the laryngeal mask: an immediately available, very quick, very easy technique that might just possibly get you and your patient out of a jam', but the instructions to contributors preclude this.

Despite anaesthetising well over 1000 patients each year, an unexpected difficult intubation is not encountered very often and we could not hope, before retirement, to validate the technique in the way apparently required by Dr Frerk. We disagree with him that 'an unrecognised oesophageal intubation is surely in most instances more dangerous than a known failed intubation'; we think it always is and hope that every anaesthetist in the UK who does not have immediate access to capnography has familiarised him/herself with the oesophageal detector device[1] as modified by Nunn[2] and has it routinely available. The recently published Maternal Mortality Report[3] advocates consideration of the use of the laryngeal mask when unexpected difficulty with intubation is encountered and our technique may be a useful extension, particularly where there is a requirement for immediate delivery.

We are somewhat concerned at an apparent tendency to 'fail safe' and label an increasing proportion of patients as impossible to intubate, thus perhaps condemning them unnecessarily to complex procedures in the future. The patient who prompted the study had caused extreme difficulty to a highly skilled and experienced colleague and was, not surprisingly, apprehensive before anaesthesia. Her gratitude afterwards was overwhelming and only at this time did she relate that she had been completely unable to eat for a week after her previous anaesthetic: she was amazed at the absence of sore throat on this occasion.

We have received one report of success from a grateful friend but would again stress that gaining familiarity with the technique on routine cases is a sensible way of maximising the chance of success; we would also reiterate that there is no point in attempting to intubate through an imperfectly placed laryngeal mask.

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Cricoid pressure and the laryngeal mask airway

I read with interest the paper by Heath and Allagain (*Anaesthesia* 1991; **46:** 545–8) regarding a technique of blind intubation through the laryngeal mask airway (LMA). Whilst this technique is to be commended, there are several issues that the paper failed to address with regard to the safety of the technique in failed intubation where cricoid pressure is maintained. Firstly, does the application of cricoid pressure reduce the ease of insertion of the LMA? Secondly, does cricoid pressure affect the final placement of the LMA, particularly with regard to the oesophagus? Finally, why does cricoid pressure make blind intubation through the LMA more difficult?

In answer to these questions, 80 patients (ASA 1–3) undergoing minor peripheral elective surgery were randomly allocated into two groups. Both groups were premedicated with temazepam, their lungs pre-oxygenated and anaesthesia was induced with propofol. Group 1 had cricoid pressure applied prior to insertion of the LMA and group 2 did not. The LMA was inserted in the normal manner using a size 3 for females and a size 4 for males and the cuff was inflated with 20–30 ml of air. If the airway was patent, as assessed by gentle hand ventilation and observation of the chest, the position of the LMA was rapidly determined fibreoptically. The position of the LMA was scored as follows as viewed from the mask aperture bars: 4, larynx only; 3, larynx plus posterior epiglottis; 2, larynx plus anterior epiglottis; 1, larynx not seen; 0, failure to insert adequately first time. Also the visibility of the oesophagus was noted. Following assessment, cricoid pressure was released and anaesthesia was continued with

Table 1.

Score	Laryngoscopic findings (%) 4	3	2	1	0	Oesophagus seen
Group 1	12	10	12	0	6	4
$n = 40$	(30)	(25)	(30)	(0)	(15)	(10)
Group 2	11	14	12	0	3	3
$n = 40$	(27.5)	(35)	(30)	(0)	(7.5)	(7.5)
Totals	23	24	24	0	9	7
$n = 80$	(29)	(30)	(30)	0	(11)	(9)

enflurane and nitrous oxide in 30% oxygen. Patients who scored 0 were managed with a facemask and the LMA re-inserted later using a variety of different approaches. Before surgery began and prior to fixation of the LMA to the face, the fibreoptic scope was re-inserted and cricoid pressure applied and any differences in the position of the LMA were noted, including displacement of the LMA at the level of the teeth.

The results are given in Table 1. Application of cricoid pressure did not significantly reduce the ease of insertion of the LMA or its position in relation to the oesophagus or epiglottis. Also application of cricoid pressure did not cause significant displacement as measured at the teeth. However, cricoid pressure did cause anterior tilt of the laryngeal outlet of between about 10 and 40° in every patient, thus making the angle of approach for a blindly passed ETT worse. This explains the increased difficulty of blind intubation through the LMA with cricoid pressure applied.

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Use of the laryngeal mask in a patient with an unstable fracture of the cervical spine

A 24-year-old man was admitted with an unstable fracture of the cervical spine at the level of C_{1-2} and a malar fracture following an assault. He had no other injury and sustained no neurological deficit. The spinal injury was treated with skull traction, callipers having been inserted under local anaesthesia. Two weeks following his admission it was decided that surgery would be needed for his left malar fracture and that further delay would be inappropriate. The patient was otherwise fit and well and had never before had a general anaesthetic. Temazepam 30 mg orally and hyoscine 0.4 mg intramuscularly were given 1 hour pre-operatively. Stability of the cervical spine was ensured with a hard collar device. On arrival in the operating theatre he was drowsy but fully cooperative. It was decided to proceed with an inhalational induction using nitrous oxide, oxygen and halothane. A size 4 laryngeal mask was inserted without difficulty. Surgery proceeded uneventfully and the airway was well maintained throughout with no cardiovascular instability or change in the haemoglobin oxygen saturation. Postoperative recovery was smooth and there was no neurological deficit. This technique avoided movement of the cervical spine and tracheal intubation. Virtually no manipulation of the airway was necessary.

The laryngeal mask has been well documented as an aid to tracheal intubation[1–4] and it has also been used in anaesthesia for repair of a cleft palate.[5] In this case it proved to be the most appropriate tool for maintenance of the airway during anaesthesia.

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Facilitation of the insertion of the laryngeal mask

When first using these masks,[1] I experienced difficulty in inserting the mask over the dorsum of the tongue into the laryngopharynx. Since then, after using the mask in more than 100 patients, I have developed the following technique to facilitate insertion.

When the patient is deep enough and sufficiently relaxed, an assistant, placing the middle fingers behind the angle of the mandible and the thumbs over the chin, exerts traction in an anterior and then inferior direction so as to produce an extra wide mouth-opening. The tube is then inserted lateral to the tongue and spiralled around to the mid-line and then down over the dorsum of the tongue until it locates in the apex of the laryngopharynx. Having done this, it is then an easy matter to slowly blow up the cuff until an adequate seal has taken place, as judged by manual inflation of the reservoir bag. A 50 ml syringe will be found to facilitate the feeling of 'end-point' for inflation by the assistant. When adequate inflation has occurred, a sudden increase in resistance will be felt, coinciding with adequacy of inflation as judged by the anaesthetist.

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Reference

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APACHE II and clinical sickness score

I would like to draw your attention to a number of errors in the paper 'A comparison of APACHE II and a clinical sickness score' (*Anaesthesia* 1991; **46:** 442–6.)

(a) The authors do not appear to appreciate the difference between the APACHE II score and the risk of death. Their definition of the APACHE II score: 'is made up of a physiological score, weighted for age, *diagnostic group* and chronic health' is incorrect. There are very important differences between the APACHE II score and the APACHE risk of death.[1,2] The former is a *summary score* based on derangement in physiology, chronic health status and age. While it is true that mortality (y-axis) increases with the APACHE II score (x-axis), the y-intercept varies according to the diagnosis. The most extreme examples are sepsis and diabetic ketoacidosis.[3] The APACHE II score does not account for case-mix and therefore cannot be used for audit or evaluation of therapy except for a narrow class of patients.

The APACHE risk of death is *probability* of dying estimated from a logistic regression equation, substituting into the equation the APACHE II score, a coefficient based on a specific diagnostic category and whether emergency surgery was performed. The logistic regression equation and the coefficients were derived from over 5000 patients.[2] It has now been validated extensively all over the world with a database exceeding 60 000 patients. The APACHE II risk of death calculated for each patient after 24 hours in the ICU is a probability. If a patient has an APACHE II risk of death of 30%, all it means is that out of 100 patients with the same diagnosis and the same degree of physiological derangement and the same amount of reserve, 30 are expected to die. Because it is based on static analysis of group data, it is generally not applicable for clinical decision making in the individual patient.[4] However, it is useful as an audit instrument. The standardised mortality ratio (SMR), which is obtained by dividing the observed by the expected mortality (where the expected mortality is the sum of the individual risks of all the patients divided by the total number of patients), for an intensive care unit (ICU) gives an indication of its performance. In general, if an ICU's SMR is less than 1 it is performing better than expected; if a unit has an SMR greater than 1.3 there may be a problem. The beauty of the system is that by recalculating the SMR,[5] excluding specific groups of patients, the problem area can be located. For example, an ICU in a tertiary hospital with large numbers of transfers has a high SMR, say 1.7. If the transferred patients were excluded in recalculating the SMR, and the new SMR is say 1.1, we can say that the performance of the ICU is adversely affected by transfer patients, a problem known as 'lead-time bias'.[6] This may be due to poor triage, deterioration during transfer, late transfers, problems at the referring ICUs or other causes. The APACHE II score, the clinical sickness score (CSS) or any other current system cannot be used in such a way.

(b) Figures 1 and 2 are meaningless. The cell sizes are too small. Also, there are obvious errors in Figure 1: with a CSS of 1, there were three ITU survivors, no ITU nonsurvivors and one hospital (postICU) survivor and yet no hospital nonsurvivor. There should have been two hospital nonsurvivors. With a CSS of 2, there was one ITU survivor and four hospital survivors, another impossibility. When there are errors in simple outcome classification how valid are the other computations in this paper?

(c) The authors used cut-off points of 18 or 20 for the APACHE II score and 13 or 16 for the CSS to estimate the sensitivity, specificity and positive predictive value of the two systems (Table 3). This methodology, although it reminds me of how one estimates the ED_{50} for a drug, has absolutely no relevance in testing the usefulness or lack of use of a system for audit. First of all, *scores* and not *probability* of death were used (see above). To be useful for audit, the system should be predictive over the entire risk range. The way to do this is to plot observed mortality against predicted mortality, a perfect system being a straight line passing through the x-y origin at 45°.

(d) Figure 3 is a futile exercise. It is like trying to compare the performance of an Intercity express train and a donkey drawn cart on a motor-way! Unless data have been collected for the CSS to enable probability estimates to be made and then *tested prospectively*, one cannot say whether it will work or not. Even then only a comparison of the areas under the receiver-operator characteristics (ROC)[2] curves of the APACHE II risk and the CSS risk may give us an idea of which is the better system.

(e) The time taken to do APACHE II assessments is grossly exaggerated. It takes an experienced data collector less than 3 minutes to do an APACHE II assessment. Meaningful audit has to be properly organised and funded. The time 'saved' in collecting data for an unvalidated system by untrained and *ad hoc* data collectors will end up as time wasted.

Finally, by sowing confusion, this paper has done a great disservice to the relatively new science of prognosis in intensive care.

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A reply

We thank Mr Chang for showing interest in our paper and drawing attention to five specific areas of our work. We are, however, disappointed that Mr Chang takes such a negative view. Clinical sickness score (CSS) was developed and evaluated in central Africa where laboratory back-up and information systems are often absent. This is likely to be the situation for the foreseeable future in most of the developing world. There is, however, no shortage of critically ill patients and an urgent need to audit the expensive resource of Intensive Care. There has been very little information so far from the Intensive Care Units of the developing world[1–4] and far from doing a disservice to prognosis in Intensive Care the continued development of CSS represents a significant advance in the audit of medicine in the Third World. It is a simple means of illness

Table. A comparison of APACHE II and a clinical sickness score

	CSS					APACHE II			
	ICU outcome		Hosp. outcome			ICU outcome		Hosp. outcome	
Score	Survivors	Nonsurvivors	Survivors	Nonsurvivors	Score	Survivors	Nonsurvivors	Survivors	Nonsurvivors
0	3	0	3	0	0	2	0	2	0
1	1	0	1	0	1	2	0	2	0
2	4	0	4	0	2	2	0	2	0
3	3	0	3	0	4	2	0	2	0
4	7	1	6	2	5	1	0	1	0
5	4	0	4	0	6	0	1	0	1
6	1	0	1	0	7	3	0	3	0
7	2	0	2	0	8	1	0	1	0
8	4	1	3	2	9	1	0	1	0
9	4	1	3	2	10	4	0	4	0
10	2	0	1	1	11	7	1	7	1
11	3	1	3	1	12	3	0	2	1
12	1	0	1	0	13	3	0	3	0
13	1	2	1	2	14	3	0	3	0
14	0	1	0	1	15	5	1	5	1
15	3	1	1	3	16	3	3	3	3
16	3	1	3	1	17	4	3	4	3
17	1	6	1	6	18	1	1	1	1
18	2	1	2	1	19	1	2	1	2
19	6	4	6	4	20	2	1	2	1
20	2	1	3	1	21	2	2	1	3
21	0	1	0	1	22	1	2	1	2
22	3	3	3	3	23	1	1	1	1
23	0	1	0	1	24	0	1	0	1
24	2	3	2	3	25	2	0	2	0
25	1	3	1	3	26	1	1	1	1
26	1	0	1	0	27	2	0	0	2
					28	2	1	1	2
					29	3	0	2	1
					30	0	3	0	3
					31	0	2	0	2
					32	0	3	0	3
					34	0	1	0	1
					40	0	1	0	1
					42	0	1	0	1
					44	0	1	0	1

severity classification which can be used in areas of the world where APACHE II may well never be used. Our comparison of CSS and APACHE II scores was a logical step in the system's development.

We appreciate the concept of risk of death and do not contend the power of the APACHE II risk of death and standardised mortality ratios. We did not mention this very important area in our paper simply because we do not have a risk of death system based on CSS and our omission certainly does not imply either ignorance or criticism.

We would like to thank Mr Chang for drawing attention to an error in our histograms. This occurred in transcription from the raw data and therefore did not in any way affect our results or conclusion. To clarify this we present our raw data in the attached table. We agree with Mr Chang that ROC curves are an elegant way of presenting data derived from a sensitivity and specificity of scoring systems. Our conclusions based on cut-offs in both scoring systems are, however, nonetheless valid.

We would also like to stress that CSS was evaluated in a large series of patients in Central Africa using techniques described by Mr Chang in his letter[5] and we would like to draw attention to the fact that we have claimed in this paper simply that both admission scores for APACHE and CSS are of modest predicted value. We have claimed no more.

Finally, it is our experience that the collection, storage and retrieval of the data required to compile APACHE II scores and to calculate APACHE II risk of death and standardised mortality ratios is extremely time consuming. This presents few problems in Intensive Care Units where staffing and resources are adequate, but in Intensive Care Units where hard pressed consultant staff are working with one inexperienced junior doctor and little else, there are simply not enough hours in the day to implement the excellent systems developed by Mr Chang and others. In the UK we hope that all Intensive Care Units will be able to join those already able to travel on an Intercity express but at present a horse-drawn cart is better than nothing. For the developing world a horse-drawn cart may well be the only thing they will ever have.

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Cost of intensive care

The timely paper by Ridley and colleagues (*Anaesthesia* 1991; **46:** 523–30) confirms other work on the cost of intensive therapy.[1–3] In 1988, our average cost per patient day was £550,[2] which has now risen to £758 for the current financial year (1991/1992), with an average cost of £2653 per patient. The cost can be broken down under four budget headings and includes staff costs (57%), consummables (19%), equipment (3%) and hidden costs (21%). Clearly the equipment budget is starved of resource, but traditionally this has provided the Health Authority with an item to squeeze to balance the financial books.

Hidden costs are an intriguing item, which represents £195 700 out of a total budget of £928 874 (1991/1992). It includes National Insurance contributions at 4% (£21 200), VAT on equipment and disposables at 17.5% (£34 500) and the fixed hospital overhead costs, e.g. rates, heat, light etc, which is calculated at £400 per patient (£140 000).

Sheill *et al.*[3] have also looked at the cost per survivor for selected diagnosis, which bear comparison with the costs in Canada[4] and Norway,[5] but not of course the USA.[6] Shiell *et al.*'s study had five patients (5%) costing more than £10 000 and a further nine (13%) between £5000 and £9999. The next step must be to try to expand this work; it is not dissimilar from knowing the cost of dialysis or a heart transplant. We are then in a position to look at the way resources are being used in intensive care and match treatment strategy, clinical diagnostic group and outcome. A multicentre study to achieve this very basic knowledge is long overdue.

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Cardiovascular effects of epidural local anaesthetics

Drs Kerkkamp and Gielen's paper comparing the cardiovascular effects of epidural ropivacaine and bupivacaine (*Anaesthesia* 1991; **46:** 361–65) is interesting in its monitoring technique, but innacurate in some parts of its methodology and conclusions.

Ropivacaine 0.75% and bupivacaine 0.75% are not of equal anaesthetic potency and thus any differences in their effects on cardiovascular parameters are not surprising. Also the addition of adrenaline to the solutions can only confuse matters if one is solely investigating the effect of a local anaesthetic. By omitting the results of an undisclosed number of patients requiring treatment for hypotension or bradycardia the authors exclude the more extreme changes in cardiovascular status which they aimed to investigate. With regard to the statistical analysis, multiple *t*-tests were applied to the data whereas analysis of variance would have been more appropriate. However, having ascertained no statistical differences between the two groups with regard to blood pressure and heart rate, the authors ignore their statistical findings and discuss why the changes are more pronounced in one group compared to the other.

In conclusion, I agree with the authors final statement that further study is warranted using plain solutions.

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Pulse oximetry in pulseless patients

We report two instances of pulse oximetry readings at variance with the physiological states of patients monitored.

The first involved an 8 kg, 3-year-old, emaciated girl suffering recurrent chest infections secondary to achalasia of the cardia. This was scheduled for surgical correction and despite premedication she was uncooperative and had poor peripheral veins. An inhalational induction and tracheal intubation was performed using oxygen, nitrous oxide and halothane. Copious oral secretions were aspirated and venous access secured while an oximeter probe (Ohmeda Biox 3700), Dinamap cuff and ECG electrodies were applied. IPPV with capnography followed administration of atracurium 4 mg. At this stage despite an Sp_{O_2} of 90% and heart rate of 130/minute, no ECG trace was displayed. This was attributed to an electrode, lead or machine fault and attempts were made to rectify this. The low Sp_{O_2} was consistent with her pre-operative respiratory function. Minutes later, after surgical preparation, an automated reading indicated hypotension which was confirmed by palpation of peripheral pulses, while capnography showed a low $F_{E'}CO_2$ (3·6 kPa). Halothane and nitrous oxide were discontinued, intravenous fluids administered and the head end of the table declined. Upon entry of the chest, despite a displayed oximeter wave form, Sp_{O_2} of 92% and pulse rate of 120/minute, the heart was found to be asystolic. Immediate internal cardiac massage and resuscitative measures established satisfactory

cardiorespiratory parameters, allowing rapid completion of surgery. However, the hypoxic episode resulted in multiple organ system failure and the child's death 24 hours later.

The second incident, 2 months later, involved a 24-year-old male, certified as brain dead and submitted for organ harvesting. His lungs were ventilated with oxygen and he received intravenous fluids and ionotropes for organ perfusion and preservation. Pre-operative monitoring of blood pressure, central venous pressure, $F_{E'}CO_2$ and Sa_{O_2} was continued. Normal parameters were maintained with a Sp_{O_2} of 98% and heart rate of 70/minute. After cardiectomy, the oximeter (Ohmeda Biox 3700) continued reading an Sp_{O_2} of 98% with a heart rate of 120/minute. The rate and waveform were dissimilar from the general pattern before cardiectomy but resembled that seen during earlier tachyarrhythmias. The readings persisted for 15 minutes while the chest was closed. Following the discussions associated with the first case, all available anaesthetists were summoned to witness the phenomenon. Despite turning off operating theatre lights and covering the digital probe with an opaque towel, readings remained unchanged. Removal of the probe resulted in cessation of readings while re-application produced a similar Sp_{O_2} but a less convincing waveform.

These two experiences confirm that the blood oxygen saturation and heart rate values of the present generation of pulse oximeters should be used with a great deal of caution[1] and suggests that evidence is still awaited to show that oximetry has contributed to a reduction in morbidity and mortality.[2] The Ohmeda Biox 3700 is an example of the current generation of oximeters which is unreliable at low oxygen saturations. Their sensitivity allows pulse detection despite inadequate tissue perfusion.[3,4] Additionally, automatic signal adjustment by the Biox 3700 provides a plethysmographic wave form to fill the screen. This may give falsely encouraging displays,[5] as appears to have occurred in our first case and which was confirmed by the second.

Awareness of these hazardous design characteristics is essential when this oximeter is used.

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A false compatibility

In this hospital patients recovering after anaesthesia with a laryngeal mask in place are given supplemental oxygen via a paediatric T-piece (Rendell-Baker double swivel connector, Warne-Franklin) without a reservoir tube. Recently I was concerned to find that a patient's oxygen tubing had been connected to the T-piece as shown in Figure 1. The swivel connector of the mask had been detached and fitted to the 15 mm connection of the T-piece. Fortunately the patient came to no harm, despite the consequent severe obstruction to respiration.

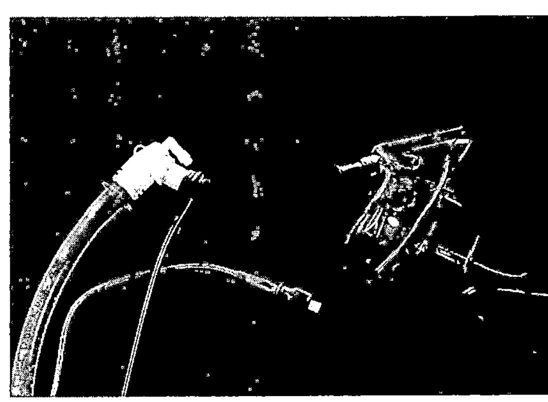

Fig. 1.

Examination showed that the detached mask oxygen swivel and the 15 mm connection fitted so well that the nurse might be forgiven for thinking that it was intended. Clearly the equipment was misused, and the manufacturers cannot be implicated, but users should be aware of this dangerous false compatibility.

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Glycopyrronium and reflex bradycardia on elevation of zygoma

Elevation of the zygoma has been reported to cause severe bradycardia[1] and glycopyrronium 0.2 mg intravenously has been quoted as being sufficient to prevent reflex bradycardia on vagal stimulation in adults.[2] I routinely administer this dose on induction of anaesthesia for any case that may involve vagal stimulation, including elevation of the zygoma. I have had no episodes of reflex bradycardia with this technique until this following case.

A fit, 70 kg, 31-year-old man was scheduled for elevation of a fractured zygoma. At induction of anaesthesia glycopyrronium 0.2 mg was administered intravenously, followed by propofol 200 mg, fentanyl 50 μg and vecuronium 4 mg. The patient's lungs were ventilated via an orotracheal tube with nitrous oxide, oxygen and isoflurane. Heart rate was stable at 60–80 beats/minute until elevation of the zygoma. The patient then became

profoundly bradycardic and no ECG complexes or pulse waveform were seen for approximately 10 seconds. Sinus rhythm then resumed spontaneously at 45 beats/minute. After a further 0.4 mg of glycopyrronium subsequent elevation of the zygoma had no effect on the heart rate, which remained constant at 80 beats/minute.

Glycopyrronium 0.2 mg falls within the manufacturer's initial dose range for adults of 0.2 mg–0.4 mg. However, in this patient, it was clear that 0.2 mg was not adequate to block reflex vagal response during anaesthesia. In future I would recommend use of the upper limit of the manufacturer's dose range in an attempt to prevent reflex bradycardia occurring during surgical procedures that may involve vagal stimulation.

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Pre-operative removal of dentures

I must agree with Drs Cobley and Dunne (*Anaesthesia* 1991; **46:** 596) that dentures should be left in place during an anaesthetic whenever possible. With the full denture it is almost always possible, but the partial denture is more prone to movement and dislocation. Women are particularly upset by the pre-operative removal of dentures. I am sure all anaesthetists have seen the edentulous woman grasping the upper end of the sheet on the theatre trolley with both hands, and pulling it towards her face. She keeps its upper edge stretched across her face just below her nose. When spoken to the woman remains silent or just mumbles a word, but tightly grips the sheet, so that her mouth is not exposed.

Nurses are taught to remove dentures routinely before surgery, so the anaesthetist must specify that a patient is to have his or her dentures left in place. I once left a bold statement on the anaesthetic record sheet that a certain patient should come to the operating theatre with her dentures. They were indeed brought, but in a denture pot held by the accompanying nurse! The nursing staff need to be informed that it can be correct to be anaesthetised with dentures *in situ*, but all staff, including recovery and ward staff, should be aware which patients do have dentures in place.

For the patient who comes edentulous to the operating theatre there is a manoeuvre of the facemask that almost always gives a good seal. Apply the mask by placing the caudal end of the mask firmly in the submental region, whilst holding the mask vertically. Then rotate the mask up into its usual position, at the same time pulling up the lax submental skin over the mandible with the caudal end of the mask. The extra soft tissue obtained from under the mandible fills the gaps that usually exists around the edges of the mask in an edentulous patient. A Guedel airway in place further improves the fit of the mask.

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We read with interest the letter by Drs Cobley and Dunne (*Anaesthesia* 1991; **46:** 596) concerning the pre-operative removal of dentures. We do have, however, some serious reservations concerning the matter. Although we agree that the dignity of patients is important, we feel that safety must be first and foremost. We believe that all dentures should be removed before induction of anaesthesia or pre-operatively in those patients who receive heavy sedative premedication.

Even in nonanaesthetised subjects there are reports of denture swallowing and inhalation. We would disagree with the suggested differential risk between partial and full dentures. Each denture needs individual assessment. How many of us are enabled to provide an educated assessment? We say this with some experience as one of the authors of this letter is dentally qualified and has spent some time in general dental practice. Whilst the stability of an upper complete denture relies upon 'suction' and the morphology of the alveolar ridge, a large number of lower dentures are dependant for retention almost entirely upon muscle tone. Anaesthesia or coma would reduce or abolish completely this retentive force. Generally speaking nocturnal denture wearers do so against the recommendations of their dentists. This advice is given partly to avoid inhalation but also to lessen the risk of developing a chronic candidal infection of the denture bearing surfaces. It must be appreciated that in every high street there are dental technicians offering repair services, common problems being midline fractures of the lower denture, loss of individual teeth, and fragments of flange that fracture off the body of the denture. Denture wearers often complain that these events occur with minimal force. What a ripe source of potential foreign bodies!

In our opinion, all dentures should be removed before the induction of anaesthesia. The use of dentures to aid airway maintenance during mask anaesthesia is surely unnecessary in present times especially with the availability of laryngeal masks.

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I was interested to read about the necessity or otherwise of removing dentures preoperatively (*Anaesthesia* 1991; **46:** 596). I agree that many women patients are extremely distressed at the prospect of denture removal, and I have anaesthetised one young woman with a partial denture whose husband was unaware of its existance! It has been my practice for several years to leave partial dentures in place for the duration of anaesthesia. The patients are happier, intubation is facilitated by the absence of inconvenient gaps, and the patient's own teeth are protected from damage by the laryngoscope falling into such gaps. Provided that the anaesthetist and recovery staff are aware that a denture is in place there is no reason to expect any problem to arise, and I am unaware of any difficulties occurring in any of my denture-wearing patients.

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I read with interest the letter by Drs Cobley and Dunne (*Anaesthesia* 1991; **46:** 596) concerning the removal of

dentures. The practice in Västerås in Sweden some 10 years ago was for patients with dentures to arrive in the operating theatre with a plastic pot pinned to their gown, bearing their identity label. When indicated, the dentures were removed and sent to recovery in the container. In 15 years practice in England only on three occasions has a patient arrived with their dentures in place. Just one of these was as a result of a patient request rather than oversight. Many requests by patients have been denied by nursing staff.

It has long been my view that this misguided practice persists due to the reluctance of the nursing profession to accept responsibility for loss of, or damage to, dentures. I would hope that a reasoned argument to senior nurses may yet result in the evolution of sound protocols leading to a turnaround of this needless practice.

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Parents do not always want to be present at induction of anaesthesia of their children

Parental presence at induction of anaesthesia has been a controversial issue for many years; authors have testified to both its beneficial[1] and deleterious[2] effects on the peri-oprative mood and behaviour of the child. Work assessing parental attitudes to witnessing induction of anaesthesia is limited.[3,4] What is available suggests that by no means all parents actively want to be present and a sizeable proportion definitely do not. An incident occurred at induction which could well have had a considerably more serious outcome, but which nevertheless left the child concerned with frightening memories of anaesthesia.

A healthy 6-year-old child who had not had any previous surgery or anaesthesia presented as a day case for myringotomies and insertion of grommets. Unless specifically indicated otherwise it is customary in this centre to withold sedative premedication from children undergoing day case ENT surgery. At the pre-operative visit where she was seen with her parents the child was calm and playful and no premedication was considered necessary. However, on arrival in the anaesthetic room, to which she was accompanied by her father she was screaming and struggling violently. A single attempt at securing venous access was, not surprisingly, unsuccessful and it was therefore decided to perform an inhalational induction. Just as the child was losing consciousness and quite without warning the father fainted and fell to the floor, hitting his head heavily on the side of the trolley. The child was very drowsy but still sufficiently aware to see this and became quite uncontrollable. The anaesthetic nurse had moved to help the unconscious father and it became impossible to proceed with the induction. Both daughter and father were therefore moved to the recovery ward, the operation having been abandoned.

When seen later having fully recovered, fortunately without injury, the father claimed that he had never really wanted to be present at induction as he had always had a fear of hospitals, and that he had only done so out of a sense of duty produced by a feeling of expectation from the nursing staff that a parent should attend. It is of paramount importance, particularly in centres where parents routinely accompany their children to the anaesthetic room, that they be assured that their presence is in no way expected and that their wishes should be sympathetically respected should they not wish to attend. The operation was successfully performed several weeks later after heavy premedication and without parental presence.

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Chickenpox pneumonia: NAB before IPPV?

We read with interest the case report of Drs Clark *et al.* (*Anaesthesia* 1991; **46:** 376–80) in which they discuss the management of chickenpox pneumonia. We have seen two similar cases in our intensive care unit within the last 6 months. In the first, a 54-year-old man, the disease was complicated by the rapid overnight onset of respiratory failure. Within 6 hours his condition had deteriorated from an orientated and cooperative patient ($Pa{O_2}$ of 8.9 kPa, $F{I}{O_2}$ 0.6) to one requiring mechanical ventilatory support ($Pa{O_2}$ 11.9 kPa, $F{I}{O_2}$ 1.0) The disease proved fatal despite aggressive treatment including tracheal intubation, IPPV with PEEP (15 cmH_2O), invasive haemodynamic monitoring, the use of inotropic agents and continuous veno-venous haemofiltration.

In the second case, a 44-year-old woman was admitted to the ICU, hypoxic ($Pa{O_2}$ of 6.7 kPa, $F{I}{O_2}$ 0.35) despite receiving oxygen via a facemask and having a respiratory rate of 50 breaths/minute. Her condition deteriorated and in an effort to avoid tracheal intubation and IPPV we used a Drager Evita ventilator in its assist mode (ASB) in conjunction with nasal facemasks (Respironics Inc.) to provide 'nasal assisted breathing'. With inspiratory pressure support of up to 35 cmH_2O at its highest level we were able to improve her $Pa{O_2}$ from 6.9 kPa ($F{I}{O_2}$ of 0.6) via a humidified mask to 14 kPa ($F{I}{O_2}$ 0.6) with a tight fitting nasal mask. She tolerated this mask initially continuously and then intermittently as she improved, for a period of 14 days. Removal of the mask in the early part of her stay in ICU was accompanied by a rapid and dramatic arterial oxygen desaturation as monitored by pulse oximetry. Arterial sampling at the time revealed a $Pa{O_2}$ of 4 kPa, ($F{I}{O_2}$ 0.6, Hudson Mask and East Blower Humidifier).

There are a number of problems with tracheal intubation

and IPPV, such as secondary chest infection, the need for sedation and the recently reported problem of laryngeal oedema specifically after extubation in chickenpox pneumonia.[1] We suggest a trial of nasal assisted breathing before IPPV and these problems, including the potential need for elective tracheostomy, may be avoided. However, we recognise that the main limitation of this technique is that the patient needs to understand and be able to cooperate with what will be, for them, an unusual form of breathing. Other advantages of this method include the preservation of the patient's morale and that of their relatives.

Interestingly in this patient the chickenpox vesicles around her nose and under the mask were much less prominent, suggesting that either the humidification or high oxygen tension under pressure was causing a regression of the vesicles.

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Higher pressure ventilation and the Bain coaxial breathing system

A 56-year-old, 85 kg, well controlled asthmatic was undergoing microlaryngoscopy, for recent onset of hoarseness. Following an uneventful induction, he was attached to a Penlon Coaxial breathing system, with fresh gas being delivered from a Boyle 2000 gas machine, and ventilated through use of a Nuffield 200 Ventilator, all of which had been previously checked and found to be functioning correctly.

Controls were set so that inflation pressures of approximately 40–45 cmH_2O were generated (fresh gas flow 6 litres/minute, inspiratory time 1 second, expiratory time 2.5 seconds, V 0.75 litres/minute), but at this inflation pressure a significant leak was noticed, during each inflation, from the expiratory valve which had been fully closed. The breathing system was immediately changed, but the same occurred with the replacement. On assessment of the patient, the procedure was continued as ventilation as shown by auscultation, capnography and pulse oximetry, was found to be adequate.

Subsequent testing of two other systems confirmed the presence of a leak under similar circumstances. On examination, all four systems appeared to be functioning correctly. Subsequent testing by Penlon confirmed our supposition that the valve was to specification, however they advised that if ventilation pressures of 40–45 cmH_2O were required with no losses, then the spill valve relief pressure would need to be adjustable to 80 cmH_2O to accommodate the early opening characteristics of the coil spring design used in the manufacture of the combined expiratory/pressure relief valve. I feel that it is important to bring anaesthetists attention to this potential problem, particularly as Penlon have made available, upon special request, a spill valve with an 80 cmH_2O relief pressure.

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P.K.T NICHOLS

A reply

We have always recognised that pressure relief valves can potentially result in airway leaks when high pressures are necessary. Setting the performance criteria for such valves is to some extent subjective, and in the case of the Penlon coaxial system, the opening pressure was selected as the weighted average value resulting from an enquiry to many anaesthetists. (Suggestions ranged from 3.5 to 10 kPa, but with a well marked peak at 6 to 6.5 kPa.)

The other vital feature of a pressure relief valve is its flow capacity. In the Mapleson D/E system when used with a ventilator, there is no elastic reservoir bag in the system, which is totally closed during the inspiratory phase. However, the oxygen flush system of the machine is connected to the breathing system at all times, and inadvertent opening of the flush control during inspiration could lead almost instantly to dangerously high pressures.

In our view it is essential to include in such systems a pressure relief valve designed and rated to deal with flush flows hence our design which is tested and set at 60 litres/minute. With these design parameters it has to be accepted that some leakage will occur at pressures below the set value, but we feel that this is a lesser evil. (The same potential problem exists when circle systems are ventilated mechanically after exclusion of the reservoir bag and we include such valves in our designs.)

We have made available valves set at 8 kPa to suit a minority of clinical needs, but 12 years experience has not caused us to consider a general change on our design which we believe to represent a balanced compromise.

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Penlon Nuffield Anaesthesia Ventilator Series 200. The case for vigilance?

During the course of a routine operating list, a previously checked and fully functioning, Nuffield Series 200 Ventilator was noted to have developed a fault. The flow control would no longer advance beyond the 0.75 litre second marking. The ventilator, which had been serviced by the company 5 weeks previously, was immediately withdrawn from service. Examination revealed that the screw used as a stop to prevent excessive rotation of the flow control had worked loose and was obstructing free rotation of the control knob against the bottom of the casing. It was also noted that should the screw have worked any looser, then the flow control could have been rotated far beyond its intended limits, with the risk of barotrauma or inadequate ventilation. I therefore believe that prior to each use, mechanical function, and accuracy of, the flow control should be checked.

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P.K.T. NICHOLS

A reply

We quite agree with Dr Nichols that a function test should always be performed before the Nuffield Ventilator is used, although this is only necessary at the beginning of each day. We also suggest that any active device be function-tested daily before use.

With regard to the safety of the flow control, the complete release of the stop mechanism permitting uncontrolled rotation is impossible. The length of the stop screw is such that before it releases control from its mating stop pin through becoming loose, it will fully obstruct onto the casing preventing out of control rotation.

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Atrial fibrillation after electroconvulsive therapy

Most arrhythmias following electroconvulsive therapy are benign. We describe a patient in whom atrial fibrillation occurred immediately after such treatment. An 84-year-old man with a depressive illness had had uneventful bimonthly electroconvulsive treatments as an outpatient for 4 years. His medical history was remarkable only for treated mild hypertension and benign prostatic hypertrophy. His blood pressure was 150/80 mmHg and pulse rate 70 beats/minute. Electrocardiographic and chest X ray findings were normal. The patient was pretreated with 0.4 mg of intramuscular atropine. After a blood-pressure cuff, pulse oximeter, and electrocardiographic monitors has been placed, he was given methohexitone 60 mg and suxamethonium 60 mg. When adequate relaxation was achieved, assisted ventilation was begun and bilateral electroconvulsive therapy administered

Immediately afterwards, a supraventricular tachycardia developed, associated with a heart rate of 180/minute and blood pressure of 170/100 mmHg. Esmolol (25 mg intravenously) was given in incremental doses, reducing the heart rate to 120/minutes and blood pressure to 160/90 mmHg. Oxygen saturation was stable at 96%, but telemetry indicated an irregular rhythm. Electrocardiography showed atrial fibrillation and a ventricular response of 120/minute persisting for 20 to 30 minutes. The patient, now alert, had no chest pain, shortness of breath, or general discomfort. Cardioversion using 100 Joules was performed after administration of methohexitone 50 mg. A normal sinus rhythm of 80 beats/minute was achieved. The patient was observed for 3 hours and discharged home. Esmolol 20 mg intravenously was used prophylactically during subsequent electroconvulsive treatments, and no abnormalities were observed.

Cardiovascular complications cause most of the medical disorders and deaths in patients undergoing electroconvulsive therapy.[1] Transient benign arrhythmias occur more often in elderly patients and patients with cardiac disease,[1,2] hypoxaemia or hypercapnia.[3] The pathophysiological changes due to the therapy may render high-risk patients susceptible to arrhythmias. A brief vagal response is followed by a burst of sympathetic activity accompanying the seizure. This activity can predispose compromised patients to myocardial ischaemia or stretching of atrial fibres, resulting in atrial fibrillation.[4] Studies in animals have shown that electrical stimulation of the brain can produce sympathetic-mediated arrhythmias, including atrial fibrillation.[5] We found only one other report of atrial fibrillation associated with electroconvulsive therapy.[6] The treatment was administered without electrocardiographic monitoring, and atrial fibrillation was detected 30 minutes later. The arrhythmia was attributed to an idiosyncratic response to suxamethonium.

Therapeutic and prophylactic efforts have focused on controlling the atrial and ventricular rates before electroconvulsive therapy. One study found that labetalol was superior to esmolol in protecting against increases in heart rate and blood pressure,[7] but that it significantly decreased seizure duration.[7,8] Studies of the effect of esmolol on seizure length have yielded conflicting results.[7,8] There have been no investigations of prophylaxis for supraventricular arrhythmias due to electroconvulsive therapy.

We considered our patient's arrhythmia to be an isolated phenomenon unrelated to an underlying cardiac disease. We treated him with cardioversion instead of pharmacological agents because we assumed that his atrial fibrillation was due directly to the haemodynamic derangements resulting from electroconvulsive therapy. Furthermore, he was an outpatient who did not necessarily require admission for control of atrial fibrillation.

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Temperature and drug potency

Unexpected or poor clinical responses to administered drugs occur in anaesthetic practice and may be difficult to explain. I discovered a potential cause for reduced drug potency by chance recently during a routine operating list. I was surprised to remove an ampoule of neostigmine from its box and find the ampoule very warm to the touch. The rest of the ampoules present were similarly warm. Investigation revealed the source of the heat to be the light

bulb present in the drug cupboard of the anaesthetic room. This light came on immediately the door was opened, releasing a spring-loaded button switch, a common arrangement found in drug cupboards. The door had to be fully closed to turn off the light, which in this case was prevented by the lock being turned to the locked position. This allowed the cupboard to be left opened for access to drugs during the list and the keys to be removed from the lock. The box of neostigmine had been stored on a shelf immediately above the light and a thermometer placed here revealed a temperature of 44°C.

Other drugs in close proximity and similarly warmed were labetolol and phytomenadione. Enquiries to the manufacturers of these drugs about their stability to heat revealed that neostigmine has been found stable at temperatures of 45°C over 12 months! Phytomenadione has been tested to 35°C without loss of potency and would probably be unaffected. However, labetalol is reported to degrade quite rapidly. At 37°C discoloration of the solution is seen and the active compound is degraded. A poor response to this vasoactive drug could thus be anticipated, which could have serious clinical implications, especially if used in a situation of urgency.

The problem has been resolved by rendering the light inoperative and this has not caused any nursing or medical problems. A compromise would be to position such a warning light away from the cupboard in question, but its presence does seem rather anachronistic and a potential source of complication anaesthetists could do without.

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Block of epidural needle by blood clots

I read with interest the letter from Dr Lim and colleagues (*Anaesthesia* 1991; **46:** 597–8) in which they describe the lack of loss of resistance to air despite entering the epidural space. They have postulated the cause to be blood clots in the epidural needle.

Their letter describes the appearance of blood at the hub of the epidural needle initially. I have observed that when this happens a small film of blood passes between the plunger and the inner wall of the syringe used to detect loss of resistance. The subsequent adhesion between the plunger and syringe causes a failure to detect a loss of resistance to air. These difficulties can be overcome by changing to a syringe filled with saline or even a wet syringe which has just been cleared of saline. I would suggest that had they used this technique they would have located the epidural space by loss of resistance before clots had time to form in the epidural needle and even displaced any blood in the needle on location of the epidural space.

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Luer lock connections—a potential hazard?

The recent tragic death of an asthmatic child which was associated with an alleged misconnection by a nurse of an oxygen line to an intravenous infusion, caused me to reflect that Luer lock connections are employed in the connections for: intravenous fluid/intra-arterial monitors; high pressure oxygen e.g. jet injectors for bronchoscopy; low pressure gas sampling/gas insufflation for laparoscopy; cystoscopy irrigation fluids.

Since the current national shortage of nurses has produced pressure to provide barely adequate 'skill-mixes' on wards, there is an increasing likelihood of wrong reconnection of detached lines which *appear* to join together easily, irrespective of function.

Is it not time that an alternative connection was introduced for high/low pressure air lines and keep Luer locks for fluid use only?

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Need for special needle for caudal block

Caudal block is one of the most commonly used regional techniques and it is particularly valuable in children. However, the failure rate is higher than with other regional methods and is more frequent in older patients. Failure is mainly due to considerable variation in the normal anatomy; the sacral hiatus can be obscured by bone, excess fat or fibrous tissue, while different degrees of sacral tilt vary the angle of entry for different individuals, and for adult males and females. The needle may be misplaced either into the posterior sacral ligament, the subperiosteum or even into the marrow.

Using an image intensifier I found that the most common cause of failure of caudal block performed by experienced anaesthetists was placement of the needle outside the sacral canal, usually posteriorly. This occurs despite the confidence expressed by the anaesthetist that the needle has been correctly placed. In my opinion these incidents could be drastically reduced by the use of proper regional block needles. The usual practice is to choose a 21 gauge venepuncture needle, with a long bevelled cutting tip which is very sharp. These needles do not allow discrimination between different tissues and deprive the operator of sensitivity to the texture of different tissues, thus causing misinterpretation of the feeling of penetration of the sacrococcygeal ligament. Also, because of the sharpness of the needle, the incidence of undesirable complications such as bloody tap and intravenous injection are high. There is even the possibility of intra-osseous injection of local anaesthetic, where blood levels will be almost as high as after intravenous injection of local anaesthetic. It is puzzling that while anaesthetists prefer to use Tuohy or Crawford needles for lumbar epidural blocks,

and short bevelled regional block needles for peripheral nerve blockade, this practice is not considered for caudal blocks which, after all, forms part of the epidural space.

Three years' experience in using 18 gauge Touhy needles for caudal block has shown them to be extremely helpful in locating accurately the caudal canal and in avoiding undesirable complications such as bloody taps. It would be extremely useful to have available a short, small size Touhy needle designed for use in caudal blockade.

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Anaesthesia for laparoscopic cholecystectomy

Greville and Clements presented a case report describing the anaesthetic management of a patient undergoing laparoscopic cholecystectomy using the Nd:Yag laser (*Anaesthesia* 1990; **45:** 944–955). The review was quite comprehensive and we congratulate them on their effort.

We recently administered anaesthesia for 65 patients who underwent laparoscopic cholecystectomy. Anaesthesia was induced with thiopentone, atropine, d-tubocurarine and suxamethonium and was maintained with isoflurane in oxygen-enriched air. The opioids have the potential to raise intrabiliary pressure and to interfere with interpretation of the intra-operative cholangiogram, thus making their administration relatively contraindicated. Our patients received ketorolac 60 mg intramuscularly following induction, or in the recovery room. Our first 10 patients appeared to have an unacceptable incidence of nausea and vomiting. Since one of the main purposes of this procedure, as pointed out by Drs Greville and Clements, is to increase early ambulation and to decrease hospital stay, it is clear that the high incidence of nausea and vomiting in the postoperative period would be counterproductive to the desired clinical and economic objectives of laparoscopic cholecystectomy. In and attempt to minimise or eliminate this complication, we have used intravenous droperidol 0.625 mg prophylactically about 20 minutes before the end of the surgical procedure. Alternatively, we have also used intravenous metoclopramide (10–20 mg) intra-operatively to decrease postoperative nausea. These measures have essentially eliminated the problem of nausea and vomiting in that patient population. The precise aetiology of the nausea and vomiting is unclear. It may be neurogenic secondary to traction on the coeliac axis, peritoneal distension with carbon dioxide or splanchnic manipulation. Gastric manipulation does not constitute a significant aetiological factor in this complication since patients have orogastric tubes inserted immediately after the induction of anaesthesia.

We would therefore like to submit that nausea and vomiting is a frequent complication seen in patients undergoing laparoscopic cholecystectomy and would suggest that intravenous droperidol or metoclopramide may be a satisfactory prophylactic measure for decreasing or eliminating this complication. We are now able to discharge the majority of our patients within 24 hours of surgery. Further, we believe that the opioids are relatively contraindicated in that patient population.

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Dangerous repairs

We report a case where an adult (size 3) Macintosh laryngoscope failed at a critical point. A repair had been performed in the hospital workshop some months previously and involved fixing the handle of the laryngoscope to the head where the blade attaches. The laryngoscope had subsequently been used regularly without difficulty and functioned well on routine pre-operative testing. However, while performing routine direct laryngoscopy for intubation in a fit 30-year-old patient for laparoscopy, the handle of the laryngoscope became detached from the blade mounting at the site of the old repair. The blade, mounting and batteries fell into the mouth of the patient while the handle struck the upper teeth, one of which was a crown. The airway was cleared and the patient's lungs ventilated by mask until a second laryngoscope was re-introduced. Fortunately the patient suffered no injury.

Fig. 1.

Figure 1 demonstrates the broken laryngoscope. A soldered joint can clearly be seen around the rim of the handle. The intensity of the heat used has deformed the central flange where electrical contact occurs. Soldering of this joint in the laryngoscope is not appropriate. The strength of such a bond is inadequate and led to a serious failure of equipment with potential injury to the patient in this instance. Despite the potential advantages in cost and speed of renovation, this equipment should not have been sent to the local workshop. Repair of vital anaesthetic apparatus should be performed only by the recognised servicing agents; alternatively, the equipment should be replaced.

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Esmolol in infundibular spasm

Right ventricular hypertrophy associated with pulmonary stenosis in a patient with tetralogy of Fallot leads to decreased pulmonary blood flow. The situation is aggravated by catecholamine-mediated spasm of the infundibulum.[1] We report a case of such spasm occurring intra-operatively and its successful management by esmolol.

A $5\frac{1}{2}$-year-old boy weighing 15 kg was admitted with the diagnosis tetralogy of Fallot, which was confirmed by cardiac catheterisation. Total corrective surgery for the lesion was planned. After premedication with morphine and atropine anaesthesia was induced with halothane in N_2O and O_2. After intravenous access, a plain 5.5 nasotracheal tube was placed with the help of pancuronium, incremental doses of morphine and diazepam. In the pre-incision period his heart rate was 100/minute, arterial blood pressure 100 mmHg systolic, central venous pressure 5 mmHg, oxygen saturation 80–85% and $P\text{ao}_2$ 7.4 kPa. Just before skin incision, supplementary doses of relaxant and anaesthetic drugs were given. Immediately after the incision his heart rate went up to 160/minute and blood pressure to 140 mmHg systolic. Oxygen saturation and $P\text{ao}_2$ decreased to 60% and 5 kPa respectively without any change in the airway pressure. Further deepening of anaesthesia and fluid administration failed to increase the oxygen saturation. These changes were considered to be due to infundibular spasm and hence esmolol 5 mg (about 350 μg/kg) was given. Effects became evident in the next 30 seconds and after one minute the haemodynamic measurements were in the normal range. Oxygen saturation increased to 80–85% with $P\text{ao}_2$ of 7.2 kPa. The rest of the procedure was uneventful and he was transferred to the intensive care unit with stable haemodynamics and without any inotropic support.

Sympathetic stimulation associated with anaesthesia and surgery, although short lived, results in haemodynamic changes, which may lead to serious complications in tetralogy of Fallot.[1] It is preferable to prevent these haemodynamic changes, but there are situations in which it may be necessary to treat the patient after tachycardia appears. Despite generous doses of anaesthetic agents, our patient did respond to skin incision. Beta adrenoceptor blocking drugs are the mainstay of the treatment for infundibular spasm, which can be precipitated by tachycardia.[2] Propranolol is the most widely used drug in this setting, but is not without its side effects especially during open cardiac surgery.[3] Esmolol has a short half-life and there was no difficulty in coming off bypass, which we could have anticipated had we used propranolol. Esmolol provides a convenient and effective treatment of infundibular spasm due to sympathetic stimulation and is ideally suitable during paediatric open heart surgery.

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Sensitivity to papaveretum in Gilbert's disease

Gilbert's disease is a benign disorder characterised by a mild, chronic and variable unconjugated hyperbilirubinaemia in the absence of liver disease or overt haemolysis.[1] It is inherited as an autosomal dominant trait and may affect as many as 2 to 5% of the general population.[2]

We would like to report two patients with Gilbert's disease who showed excessive sensitivity to small doses of papaveretum. The first patient was a 42-year-old 62 kg female who received papaveretum 10 mg during a total abdominal hysterectomy, who postoperatively was excessively sleepy with pinpoint pupils and a respiratory rate of 8 breaths minute. During a 6-hour stay in the recovery room, she gradually became more awake and her respiratory rate increased to 12 breaths/minute. On the ward she remained quite sleepy for 24 hours and no further doses of papaveretum were required for postoperative analgesia. The second patient was a 54-year-old 84 kg man who recieved papaveretum 10 mg during the course of an operation to repair his right inguinal hernia. Postoperatively he was very sleepy with a respiratory rate of 6 breaths/minute. Naloxone 0.1 mg given intravenously resulted in a reversal of sedation and an increase in the respiratory rate to 12 breaths/minute. Three further doses of 0.1 mg of intravenous naloxone were required over the next 4 hours to maintain an adequate respiratory rate. In view of the exaggerated response to the initial dose of papaveretum postoperative analgesia was provided with 75 mg of intramuscular diclofenac 12 hourly as required.

These are, to our knowledge, the first case reports of increased sensitivity to small therapeutic doses of papaveretum in Gilbert's disease. There has been one report of a prolonged and exaggerated effect to morphine; however, this patient weighing 75 kg had undergone cardiac surgery and received a total of 110 mg of morphine during the procedure and a further 10 mg postoperatively[3] Papaveretum is a preparation containing the water soluble alkaloids of opium, standardised to contain 50% anhydrous morphine. The other alkaloids are mainly papaverine, codeine, narcotine and thebaine. Therefore, the major active ingredient is morphine; the other alkaloids exert minimal analgesic and sedative effects. Morphine is metabolised by two major pathways, N-demethylation to normophine and formaldehyde and conjugation with glucuronic acid forming morphine-3-glucuronide and morphine-6-glucuronide, the former being the major metabolite.[4] In Gilbert's disease there is impaired uptake of bilirubin into the hepatocytes together with a deficiency of bilirubin glucuronyl transferase. Present evidence suggests that both morphine and bilirubin share the same conjugation process which includes both uptake into the hepatocytes and subsequent conjugation with glucuronic acid.[3] This may account for the exaggerated responses seen to morphine and papaveretum in patients with this disease.

Anaesthetic consideration in Gilbert's disease must include the cautious usage of opoid drugs undergoing conjugation reactions with glucuronic acid (e.g. morphine

and papaveretum). Additionally, it is important to be aware of the factors increasing the unconjugated bilirubin levels, thus worsening the jaundice, namely stress, infection and fasting. These may be minimised by adequate pre-operative assessment and premedication, aggressive treatment of infection and reducing the period of starvation by placing the patient first on the operating list and setting up an intravenous infusion containing glucose.[5]

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Wound infiltration and Caesarean section

In their paper on wound infiltration following Caesarean section (*Anaesthesia* 1991; **46:** 404–7) Dr Trotter and colleagues used patient controlled analgesia (PCA) as their escape analgesia to assess the effect of the technique. However, they also state'... escape analgesia in the form of intramuscular morphine was available...' to be used presumably if PCA didn't work. If the analgesia provided by PCA was inadequate, surely the appropriate response would be to re-assess the analgesic technique and not just give more opioid by a less controlled method. It would be impossible to predict how much the patient would require and could well lead to an overdose.

In our hospital the use of intramuscular opioids is strictly forbidden when PCA is or has recently been used. There are many reasons why PCA (or any other analgesic system) might be failing: nausea and vomiting, patient ignorance, misprogramming, anxiety etc. Therefore analgesic failure needs proper analysis and not just a 'blanket' prescription.

On a wider issue, I wonder if it is logical to use intramuscular analgesia in research nowadays. There are no studies which quantify its safety; it is impossible to estimate the correct dose for a particular individual; it is a route that may have variable absorption after surgery. Perhaps ethics committees should look closely at this means of analgesia when included in a research protocol.

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Great Yarmouth NR31 7EB

W.G. Notcutt

A reply

Dr Notcutt's interest in our paper is particularly welcome in view of his wide experience with patient-controlled analgesia in a district general hospital. In the investigative setting, the role of patient-controlled analgesia has been well established as a mechanism to assess the effectiveness of another regimen.[1] We and others have used this technique in this respect on a number of occasions. If analgesia provided by PCA is inadequate, this may of course be a result of the patient's requirements being dictated by the side effects of the drug and not by pain *per se*. Factors other than the minimum effective analgesic concentration may dictate demand.[2]

In the early days of utilising this method, it was clearly felt that some form of established analgesia should be guaranteed to the patient in the event of technical failure. Indeed, this was established in order to reassure the Ethics Committee that analgesia would be provided! No patient in our study required this intervention. Now that more enlightened times have arrived, we can regard such practices in retrospect as unnecessary and we agree with Dr Notcutt that it is probably illogical in the 1990s to use intramuscular anagesia as a research tool.

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T. Trotter
D. Fell

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It would have been the anaesthetist's fault

I have just seen Dr N.W. Goodman's letter (*Anaesthesia*, 1991; **46:** 324–5) and I agree it is too easy to ascribe causation of a death or postoperative problem to a coincidental anaesthetic. The following cases illustrate how medicolegal difficulties from 'error–blame mentality' was avoided by sheer luck.

Case 1. After spending the evening in a public house, a woman drove her car off the road, and she was taken to hospital unconscious. Since she had been 'passed' by the neurosurgeons, the maxillofacial surgeons decided to repair her fractured mandible, which was her only apparent injury. Two days later she had not recovered consciousness and an EEG showed diffuse hypoxic brain damage. The only reason that this was not immediately attributed to anaesthetic error was because no anaesthetic had been given. The fact that in Accident and Emergency (A and E) she could tolerate a tracheal tube had suggested more than just alcohol. The assignment of blame for the brain damage caused acrimony between the neurosurgical and A and E departments, when in fact it had probably been caused by airway obstruction after the accident and before the ambulance arrived.

Case 2. While premedicating the patients for one operating list, it was noted that the proposed second patient had had a period of cardiovascular instability for most of the morning, although this had settled by mid-afternoon. The operation was postponed for a few days to ensure that the instability would not recur. The next day the replacement second operation was well underway when a telephone message was received from the ward that the cancelled patient had had a cardiac arrest. Resuscitation was unsuccessful. Without the postponement, what odds on the anaesthetic being blamed?

Like Dr Goodman, I believe that association and causation are too often confused, and this applies in all branches of medicine.

Princess Margaret Rose Hospital
Edinburgh
E.L. LLOYD

Isoflurane field anaesthesia at extreme temperatures

Correspondence by Tighe, and in reply by Restall and Johnson (*Anaesthesia* 1991; **46:** 319–21) is relevant to a laboratory study of three vaporizers recently completed by us: the Penlon OMV Tri-service (OMVT), British Oxygen Company Goldman (GM) and Cyprane Isotec-3 (TEC).

At a given temperature from −1 to 45°, TEC isoflurane output was independent of plenum gas flows (2, 4, or 6 litres/minute). This independence was lost by 55°C, when, for a flow of 2 litres/minute for at least 10 minutes, all settings from 0–5% inclusive gave outputs greater than 12%. At 4 litres/minute the output again was uncontrollable (7% at all settings). At 6 litres/minute, the output percentage was close to the set percentage, except for 0, which produced 4% vapour. Set to 'off' and left hot for 9 hours with no gas flow, the TEC lost all the liquid isoflurane in its reservoir, presumably by evaporation through seals incompetent at that temperature.

In contrast, OMVT and GM outputs were controllable, at flows of 2, 4 and 6 litres/minute, plenum and drawover. Set at 0, its 'off' position, and left hot for 9 hours, OMVT did not lose any reservoir contents, (GM, like TEC, became dry in its 'off' setting).

The Triservice Apparatus can enable isoflurane anaesthesia at the 45–53°C recorded in Dr Restall's Middle Eastern operating theatres, whereas the Cyprane Isotec-3, from our data, cannot be recommended.

Launceston General Hospital,
Launceston,
Tasmania 7250
C.G. MERRIDEW
S.J. FRASER

The Humphrey ADE breathing system and ventilator alarms

The Humphrey ADE breathing system with 15 mm parallel tubing is recommended for use in adults and children for spontaneous and controlled ventilation. We have found that when a Penlon Nüffield ventilator is used with such an ADE breathing system, a Penlon IDP ventilator disconnection alarm connected to the inspiratory limb of the system may fail to provide warning of disconnection from the tracheal tube. High flows generated by the Penlon Nuffield ventilator produce sufficiently high and sustained pressures within the breathing system to cycle the IDP alarm, even if disconnection has occurred. Using a flow of 750 ml/second and an inspiratory phase of 1 second, the Penlon IDP pressure failure alarm failed to detect disconnection from the patient end. A Blease Nightingale alarm in the same position required the minimum pressure setting to be as high as 15 cmH_2O to ensure warning of disconnection was given.

A recent paper on ventilator disconnection alarms emphasises the need to show that the ventilator alarm within a system is functional by means of a trial disconnection at the tracheal tube.[1] We would support this advice and would encourage colleagues to use ventilator alarms in which the minimum pressure setting can be correctly adjusted when using the Humphrey ADE breathing system for controlled ventilation.

Leicester Royal Infirmary,
Leicester LE1 5WW
P.J. MURPHY
P.G. RABEY

Reference

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The potential hazards of using iodine as an antiseptic solution

Many thousands of invasive procedures are performed each year by anaesthetists, including epidural catheter and central line insertion. It is essential that the risk of introducing infection during these commonly performed procedures is kept to a minimum. Routine precautions taken include preparing the patient's skin with an antiseptic solution. Various germicidal solutions are available, but amongst the most commonly used is iodine.[1,2] Although the occurrence of skin sensitivity reaction with iodine is a well known, if relatively rare complication, other potential complications of the use of iodine are less well known. We wish to report potential hazards when using iodine in conjunction with the aluminium containers that are commonly supplied in hospital invasive procedure packs, (Fig. 1).

Powdered aluminium reacts with iodine very vigorously and this reaction is catalysed by water. Addition of water to a mixture of iodine and aluminium causes the mass to burst into flame. This reaction occurs as follows:

$$2Al + 3I_2 \rightarrow 2AlI_3$$

$$2AlI_3 \xrightarrow{3H_2O} Al_2O_3 + 3HI$$

Fig. 1.

Therefore if iodine is placed into aluminium pot containers before its application to the patient's skin, as is common practice, there is the potential for fire. This may be a risk not only at the time of the procedure but also later when aluminium containers contaminated with iodine residues may cause a fire in a waste bin. Furthermore, if solutions of iodine are stored in aluminium containers for any length of time the aluminium iodide generated could damage the patient's skin by virtue of the halide hydrolysing to give hydriodic acid. Indeed this process may be responsible for at least a proportion of patients who have a skin reaction to iodine often labelled as an allergic response.

In conclusion we would recommend that solutions of iodine should not be stored or handled in aluminium containers. Other antiseptic solutions such as 0.5% chlorhexidine in alcohol may be safer to use, as would the use of plastic rather than aluminium containers.

Shackleton Dept. of Anaesthetics, S.W O'KELLY
Southampton General Hospital
Professor of Organic Chemistry, P.J. PARSONS
The University of Reading

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Safety Action Bulletin

Resuscitators: regular testing and inspection SAB(91)46
Users are reminded that resuscitators should be kept in good working order and assembled and tested according to the manufacturers instructions. There have been a number of reports of cleaning and/or servicing by nontechnical staff which has resulted in incorrect assembly of components and damage to valves.

Anaesthetic vaporizers: maintenance SAB(91)47
Incidents continue to be reported despite advice in 1984, 1986 and 1988. Vaporizers must be tested and serviced regularly and users are reminded that vaporizers require careful storage, handling and protection from mechanical shock. Whenever damage to a vaporizer is suspected, even in the absence of physical signs, the vaporizer must be removed from use and returned to the manufacturer for checking. Users are reminded to test for leaks each time a vaporizer is fitted to an anaesthetic machine. Ohmeda Excel and Modulus anaesthetic machines are fitted with location pins in the backbar to prevent use of Tec 3 vaporizers. Tec 4 and Tec 5 vaporizers have an interlock system to prevent simultaneous administration of more than one volatile agent. Some hospitals have requested that the vaporizer location pins on the Excel machine be taken out so that Tec 3 vaporizers can be used. In future these pins will be made permanent.

Anaesthetic machines fitted with Penlon vaporizer off-line hoses: replacement hose assemblies SAB(91)48
Penlon vaporizer opaque off-line hoses, particularly those made from white opaque nylon plastic, used on some Penlon, Blease and M&IE anaesthetic machines have fractured near to the vaporizer connections. Replacement transparent hose assemblies are available from the appropriate anaesthetic machine manufacturers, or will be fitted at the next scheduled service, free of charge.

Hewlett-Packard, Defibrillators/Monitor battery-powered models 43100A, 43110A, 43120A and monitor model 43200A: product safety alert and publication change notices SAB(91)49
A Product Safety Alert has been issued on the above equipment relating to the detection of the KI Relay failure and early detection of the Energy Selection Switch failure. Some 43100A, series defibrillators may remain with power on after supposedly being switched off. This is generally due to failure of the relay identified as KI after extended use. This will cause battery depletion.

Hazard Notice

Handley Clockwork Syringe Driver: Fatal Incident HC (Hazard)(91)12
A Handley clockwork syringe driver was used to administer diamorphine over a 12 hour period. A serious malfunction of the device resulted in a fatal overdose. The malfunction was caused by internal damage due to the device being dropped. These syringe drivers should only be used as heparin pumps as they do not have any intrinsic safety feature. Any device that has been dropped must be taken out of service immediately.

Babytherm 4200 Infant Warmer: Risk of electrical fire. HC(Hazard)(91)13
An electrical fire in a Babytherm 4200 infant warmer resulted from the failure of soldered connections and consequent overheating of a printed circuit board. Where this equipment is in regular use and there is no provision for routine maintenance, arrangements should be made for Draeger Ltd to inspect the condition of these units.

Evaporation of diethyl ether: explosion and fire hazard HC(Hazard)(91)14
An incident has been reported in which ether vapour accumulated within a fume cupboard, which had not been switched on. The vapour was ignited by a spark from an electrically operated water bath, causing a fire. Readers are reminded of the dangers of using electrical equipment in the presence of ether and their attention is also drawn to Health Notice HN(Hazard)(85)1.

THE ASSOCIATION OF ANAESTHETISTS OF GREAT BRITAIN AND IRELAND

APPLICATION FOR MEMBERSHIP

to

The Association of Anaesthetists of Great Britain and Ireland
9 Bedford Square,
London WC1B 3RA, England

(*This application will be considered by Council at its next meeting. NO MONEY should be sent in the meantime. After acceptance of the application by Council, the Hon. Secretary will notify the applicant of Council's decision and the amount of subscription payable in the current financial year.*)

......................19

To the Honorary Secretary,
Association of Anaesthetists of Great Britain and Ireland

I (full name) .... offer my name as a candidate
BLOCK LETTERS

for (a) ORDINARY MEMBERSHIP (b) OVERSEAS MEMBERSHIP (c) ASSOCIATE MEMBERSHIP (d) TRAINEE MEMBERSHIP of the Association (*please delete categories not applicable*)*

I hold the following appointment(s) as an anaesthetist (*please state grade if in the National Health Service, and indicate the approximate proportion of time spent in the practice of anaesthesia*):

....

....

....

Qualifications (with dates)..

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(Signed)...
Address..
....Hospital Tel. No:..................................
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We, being Members† of the Association, nominate as a candidate for ORDINARY MEMBERSHIP/OVERSEAS/ASSOCIATE/TRAINEE MEMBERSHIP

....

1. (Signed)...
(NAME IN BLOCK LETTERS)
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2. (Signed)...
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* See the reverse of this page for details of membership categories.
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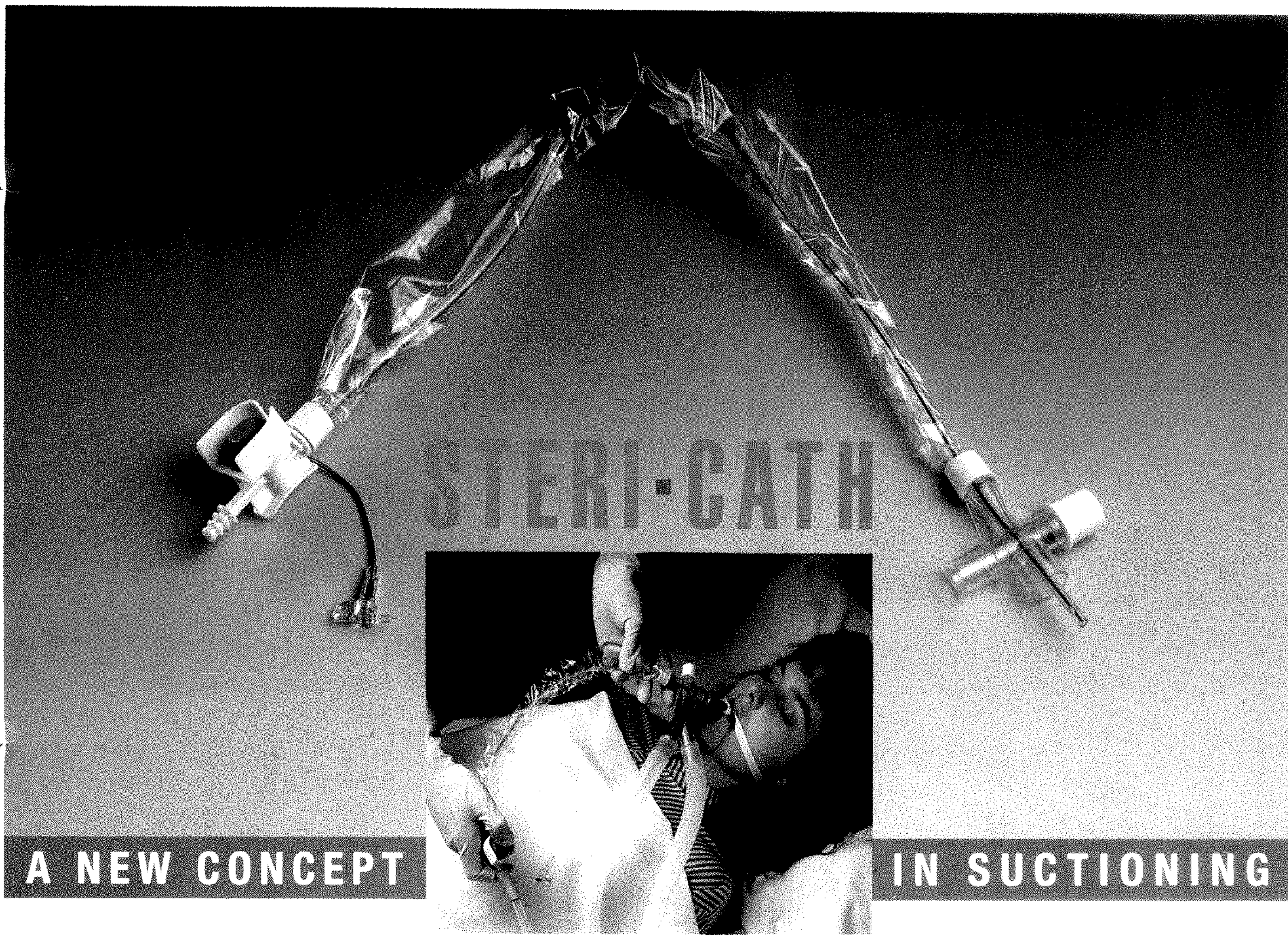

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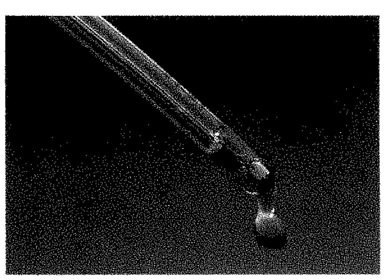

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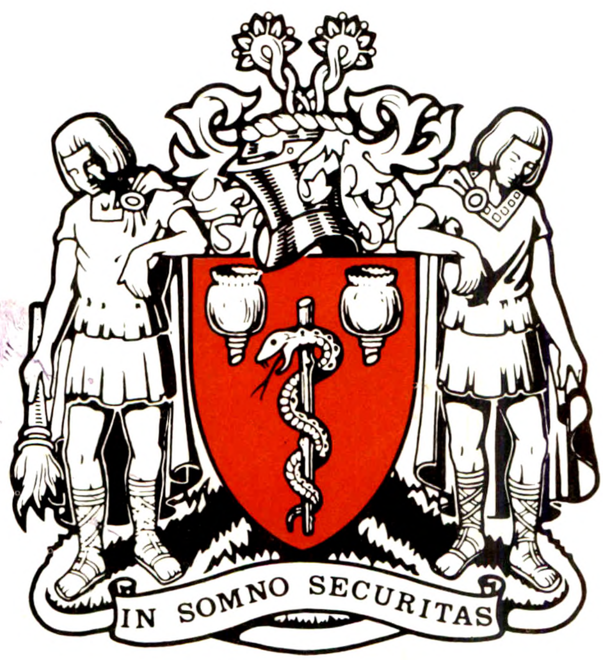

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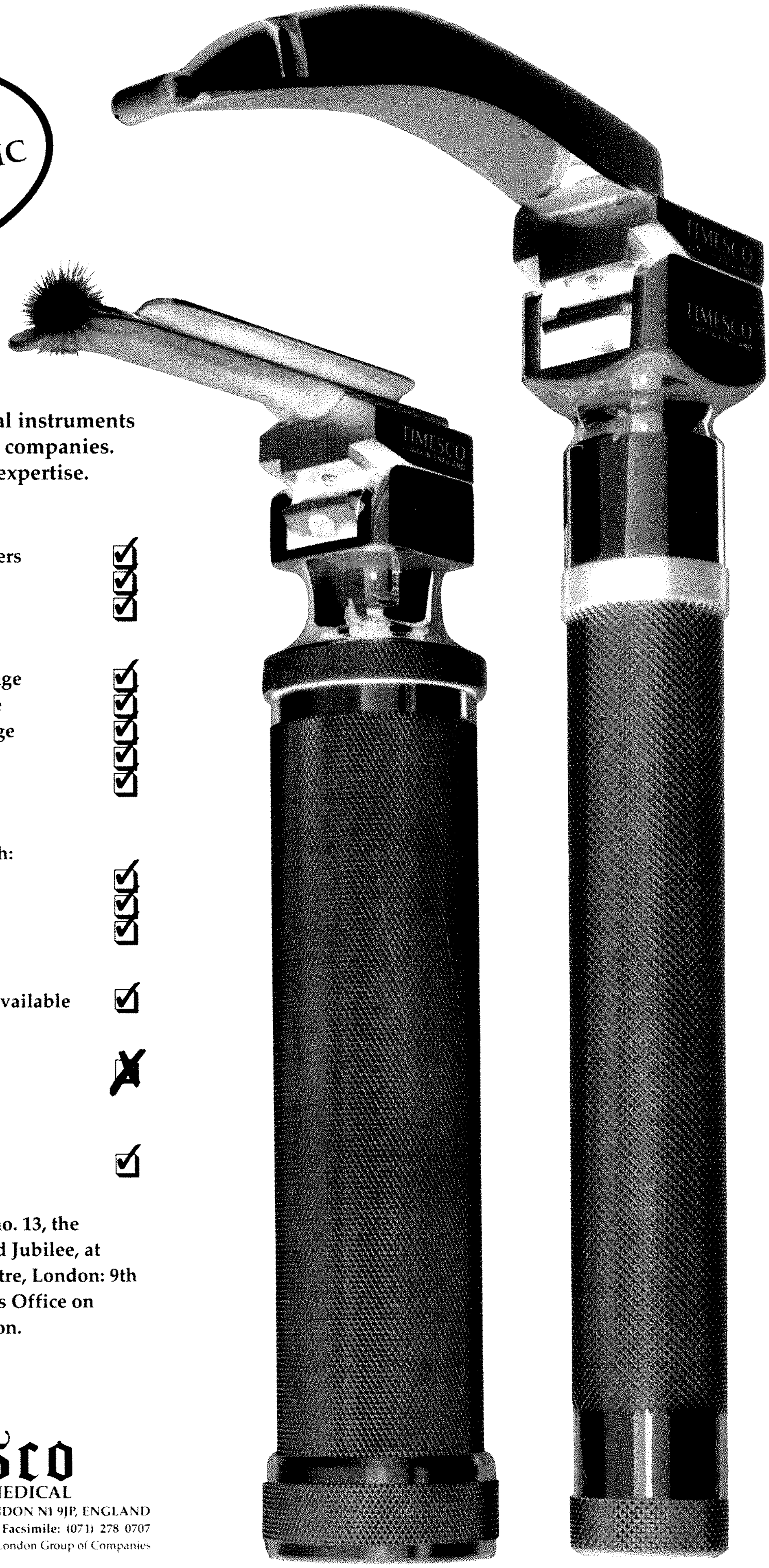

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Anaesthesia, 1991, Volume 46, pages 1003–1004

Editorial

Clonidine—a horse or an ass?

There has been an explosion of papers on the use of clonidine in anaesthesia in the last 5 years. In man, clonidine has been demonstrated to promote sleepiness but not sleep, to potentiate analgesia without being an analgesic and to reduce anaesthetic requirements without itself producing anaesthesia. Given its centrally mediated sympatholytic actions, it attenuates the autonomic responses associated with laryngoscopy and tracheal intubation and surgical stimuli. It modifies postoperative 'shivering' after volatile anaesthetics and epidurals[1,2] and muscle rigidity associated with alfentanil and sufentanil.[3] When given either intrathecally or extradurally, clonidine potentiates and prolongs the duration of concomitantly administered narcotics and local anaesthetics, although without these agents, its analgesic effects are negligible and unreliable. In their comprehensive review of $alpha_2$ adrenoceptor agonists in anaesthesia, Maze and Tranquilli[4] reviewed the pharmacology of this fascinating group of drugs and enthuse about their potential as pharmacological probes to provide insight into the many possible mechanisms of analgesia and anaesthesia. However, they conclude with the cautionary admonition about this class of compounds that 'when the dust settles we shall see whether we are riding a horse or an ass'.

It was against this background that the seminar on clonidine and $alpha_2$ agonists recently held at Bedford Square considered the clinical utility of these drugs in anaesthesia. Perhaps the most perplexing aspect of the clonidine story is not that its usefulness has suddenly been discovered but why it took so long? $Alpha_2$ agonists are probably the most commonly used adjunctive agents in veterinary anaesthetic practice. Metomidine and xylazine have been used in large quantities in veterinary and laboratory anaesthesia for many years. Maze and Tranquilli[4] estimate over 7 million animals receive $alpha_2$ agonists during anaesthesia each year. It seems at first sight strange that a class of drugs that has found ready and wide ranging acceptance for anaesthetising animals should be so slow to find an equally important place in human anaesthesia. Some of this may be due to the ubiquitous presence of more potent and selective $alpha_2$ agonists such as xylazine and metomidine in veterinary anaesthesia compared to clonidine with its mixed $alpha_1$ and $alpha_2$ effects, or to the more ready acceptance of a marked hypertensive response frequently produced in animals that might preclude their use in man. However, early reports with the potent highly selective $alpha_2$ agonists, such as dexmedetomidine, do not yet point to clear advantages or give hope that they will deliver the anticipated anaesthetic paradigm.[5]

What then is the place of the $alpha_2$ agonists in anaesthesia? As a premedicant, clonidine in a dose of 300 μg produces desirable anxiolytic, hypnotic and antisialagogue effects but this may be accompanied by an unacceptable incidence of hypotension and bradycardia.[6] Its use as a bolus dose of 3–5 μg/kg before anaesthesia reduces the anaesthetic and narcotic requirements by 40%.[7] It lessens the autonomic response to intubation and reduces haemodynamic lability during anaesthesia.[8] However, its usefulness in depressing autonomic response in clinical anaesthesia has been questioned.[9] Whilst one can think of occasions when clonidine might be helpful to reduce the quantities of anaesthetic and analgesic agents during anaesthesia, its widespread acceptance for this purpose seems unlikely. Clonidine is more likely to find a place in reducing the dose of narcotics required to control postoperative pain, but the price to be paid for less respiratory depression and nausea from the opioids is likely to be a sleepy patient.

Spinal and epidural administration of clonidine alone produces inconsistent results. However, there is general agreement as to its utility in prolonging and potentiating the effects of simultaneously administered local anaesthetics and opiates.[10,11] It has been found to be especially useful in preventing tachyphylaxis and overcoming tolerance to spinal and epidural drugs used to control chronic pain.[12]

Clonidine is an agent with many actions which may help elucidate the pharmacology of the anaesthetic state. It influences anaesthesia and analgesia. However, to date, it remains a fascinating drug awaiting a suitable anaesthetic condition to treat.

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Editorial notices

Manuscripts must be submitted in accordance with the internationally recognised *Uniform requirements for manuscripts submitted to biochemical journals* (*British Medical Journal* 1979: **1:** 432 5). Details will be found in the Notice to Contributors to *Anaesthesia* at the end of this issue.

Anaesthesia, 1991, Volume 46, pages 1005–1008

Predicting difficult intubation

C. M. FRERK

Summary

Two pre-operative tests for the prediction of difficult intubation are assessed. A modified Mallampati test and a measurement of thyromental distance were performed at the pre-operative visit of 244 patients whose tracheas were subsequently intubated under general anaesthesia. Patients in whom the posterior pharyngeal wall could not be visualised below the soft palate, who also had a distance of less than 7 cm between the prominence of the thyroid cartilage and the bony point of the chin proved significantly more likely to present difficulty with intubation. The performance of these two simple tests on all patients before operation should allow the majority of cases of difficult intubation to be anticipated.

Key words

Intubation, tracheal; complications.
Anaesthesia; evaluation, pre-operative.

Patients die every year as a result of failed tracheal intubation. The Confidential Enquiries into Maternal Deaths indicate that on average three healthy pregnant women die each year solely as a result of difficult or failed intubation.[1,2] The report on the Confidential Enquiry into Peri-operative Deaths (CEPOD) published in 1986 revealed that of the 4034 deaths reported, six involved a significant contribution from difficult or failed intubation. Worldwide, up to 600 people are thought to die each year from difficulties with intubation.[3] Any test which can predict difficult intubation at the pre-operative visit may save lives, as a result of planned use of local or regional techniques, or by allowing time to organise special procedures such as fibreoptic laryngoscopy.

It has been suggested that difficult direct laryngoscopy is associated with certain anatomical features, measurement of which can be made from X rays of the mandible and cervical spine;[4] however, it is not feasible to do these on all patients before surgery. The existing bedside tests, such as Patil's measurement of thyromental distance,[5] the Mallampati test[6] and the Wilson scoring system,[7] have been shown in various studies to have high false-positive rates, which detracts from their usefulness.[7,8] There is a need therefore, for a test that is quick and easy to perform at the bedside, that is sensitive (so that the majority of difficult cases can be identified) but is also highly specific (so that the false-positive rate will be low when the test is used routinely).

The aim of this study was to assess the usefulness of two simple pre-operative tests to predict difficult intubation, the null hypothesis being that neither test was useful.

Method

Two hundred and forty-four adults (143 men, 101 women, aged 18–82 years, mean 44.3 years) who required tracheal intubation as part of their anaesthetic were assessed before operation using two tests.

The first was a modified Mallampati test similar to that used by Samsoon and Young.[9] The seated patient opens his mouth as wide as he can and protrudes the tongue as far as possible, while the observer looks from patient eye-level and inspects the pharyngeal structures with a pen torch. It is important when performing this test that the patient does not phonate since this can alter what is seen.[10,11] The view is then graded: I, soft palate, uvula and pillars visible; II, pillars obscured by base of tongue but posterior pharyngeal wall visible below soft palate; III, soft palate only visible; IV, soft palate not visible (Fig. 1). It is important to note that, in grade III, the posterior pharyngeal wall is not visible.

The second test performed at the pre-operative visit was the measurement of the thyromental distance, with the head fully extended on the neck (Fig. 2). The distance is measured between the prominence of the thyroid cartilage and the bony point of the chin. It is important when

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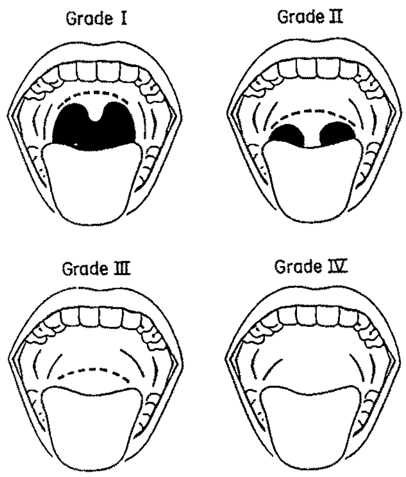

Fig. 1. Pictorial classification of the pharyngeal structures visible when performing the test, modified from Samsoon and Young.[9] Note: grade I and II posterior pharyngeal wall visible below soft palate, grade III and IV posterior pharyngeal wall not visible.

performing this test to ensure that the head is maximally extended on the neck since this ensures reproducibility, and also gives a measure of head extension, which is thought to be another factor of importance in determining the ease or difficulty of intubation.

After induction of anaesthesia and administration of myoneural blockers (using a technique appropriate for the individual patient and particular clinical circumstances), laryngoscopy was performed using a Macintosh blade and the best view obtained was noted according to Cormack and Lehane:[12] 1, vocal cords visible; 2, only arytenoids or posterior commissure visible; 3, only epiglottis visible; 4, no glottic structure visible. A note was also made of whether or not intubation was difficult, that is, if the view at laryngoscopy was grade 3 or 4 or if a gum elastic bougie was required for intubation.

Results

Of the 244 patients there were 11 who proved to be difficult to intubate (Table 1). Figure 3 shows the frequency distribution of pharyngeal gradings within the sample. It can be seen that a greater number of difficult intubations are associated with the higher pre-operative pharyngeal grades, particularly grades III and IV.

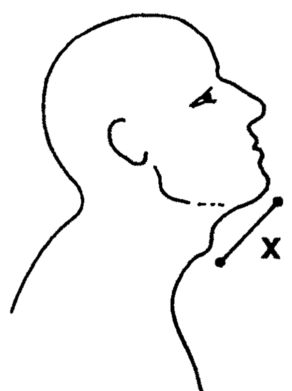

Fig. 2. Measurement of thyromental distance from the prominence of the thyroid cartilage to the bony point of the chin, with the head fully extended on the neck.

Table 1. Pre-operative test results and laryngoscopic views of patients who proved to be difficult to intubate.

Patient	Pharyngeal grading	Thyromental distance	View at laryngoscopy
1	IV	4.5 cm	4
2	III	6.6 cm	3
3	IV	7.0 cm	3
4	II	3.9 cm	3
5	IV	5.4 cm	2
6	IV	5.6 cm	2
7	III	5.8 cm	2
8	III	5.9 cm	2
9	III	6.0 cm	2
10	III	6.9 cm	2
11	II	8.5 cm	2

Table 2. The predictive value of pharyngeal grading alone, taking a grade III or IV view of the pharynx as a predictor of difficult intubation.

	Suspected to be difficult	Difficult cases picked up	False-positive results
Number of patients	52/244	9/11	43

Sensitivity 81.2%
Specificity 81.5%

Table 3. The predictive value of thyromental distance alone taking a distance of 7 cm or less as a predictor of difficult intubation.

	Suspected to be difficult	Difficult cases picked up	False-positive results
Number of patients	53/244	10/11	43

Sensitivity 90.9%
Specificity 81.5%

Figure 4 shows the frequency distribution of thyromental distances within the sample. It can be seen that a greater number of difficult intubations are associated with the shorter thyromental distances, particularly those of less than 7 cm.

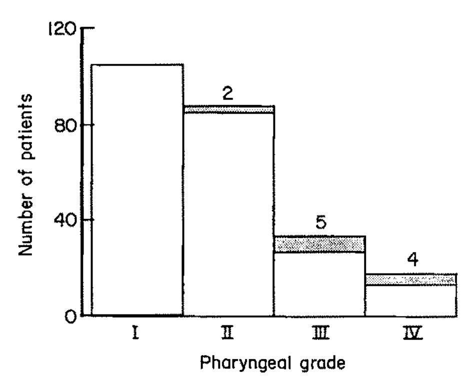

Fig. 3. Distribution of pre-operative pharyngeal gradings within the sample. (Shaded areas represent the difficult intubations.)

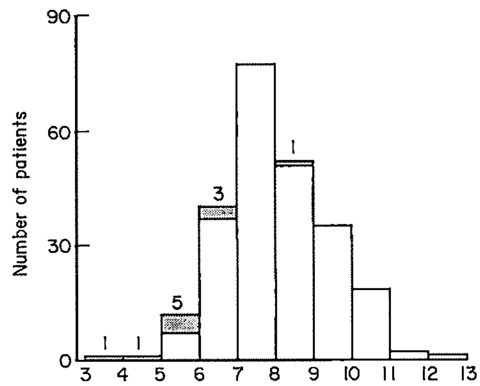

Fig. 4. Distribution of thyromental distances within the sample. (Shaded areas represent the difficult intubations.)

When the usefulness of the two tests is assessed it can be seen from Table 2 that the modified Mallampati test used on its own is sensitive, but the high number of false-positive results (false alarms) means that the test is not specific enough for routine use. One in five of all intubations that were predicted to be difficult turned out to be easy. Thyromental distance on its own is even more sensitive (Table 3), but once again the number of false-positive results means that the test is not specific enough for routine use. One in five of the patients selected on this test resulted in a false alarm.

Both tests when used alone yield many false-positive results and it has been suggested that one of the main reasons why the tests have not become widely adopted is the high false alarm rate.[8] However, if difficulty is predicted only in those patients who have both risk factors (thyromental distance of 7 cm or less and grade III or IV view of the pharynx, Table 4, Figure 5) specificity can be greatly improved (only one in 50 patients gives a false alarm) but the tests remain sensitive. When the data are analysed using the Chi-squared test, the null hypothesis can be rejected ($p < 0.01$).

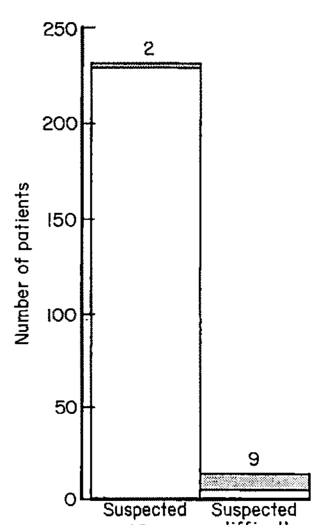

Fig. 5. Histogram showing patients who had both risk factors (thyromental distance 7 cm or less and grade III or IV view of the pharynx, suspected 'difficult') and patients who had neither risk factor or only one (suspected 'easy'). Shaded areas represent the difficult intubations.

Table 4. The predictive value of the two tests combined. A thyromental distance of 7 cm or less in a patient with a grade III or IV view of the pharynx was used as a predictor of difficult intubation.

	Suspected to be difficult	Difficult cases picked up	False-positive results
Number of patients	14/244	9/11	5

Sensitivity 81.2%
Specificity 97.8%

Since the number of patients with difficult intubation encountered in a study of this nature is small, a retrospective study of 23 cases of difficult or failed intubation which had occurred in our hospital was undertaken. The aim was to obtain a more accurate assessment of the false-negative rate when the two tests were used in combination. Eighteen of the 23 patients had both a grade III or IV view of the pharynx and a thyromental distance of 7 cm or less, giving a sensitivity of 78%, which compares well with the figure obtained in the prospective study.

Discussion

The majority of anaesthetists rely on predicting difficult intubation mainly as a result of the impression gained from the end of the bed. The limitations of this method can be seen by the fact that each year patients still die from problems associated with unexpected difficult intubation.

If a screening test such as this is to be useful, it must be performed on all patients who might need to be intubated; it must therefore be quick to perform and also give reliable results. No screening test can be 100% sensitive, therefore it is inevitable that some difficult cases will be missed, but they should be as few as possible. It is more important, however, that people do not become disillusioned with the test and abandon it altogether; thus the number of false alarms must be kept to a minimum. In this study, the tests described fulfil these criteria. With a 7 cm marker (the author uses a pencil cut to this length) it is easy to see if the thyromental distance is greater or less than this distance.

One of the greatest criticisms of the Mallampati test, however, has been the problem of interobserver variation.[13,14] Provided that the patient is not gagging or phonating, the view should be constant and a clearly defined grading system should make the test results more reproducible (Fig. 1). If the posterior pharyngeal wall can be seen below the soft palate, the patient is a grade I or II and should be 'easy'. If the posterior pharyngeal wall cannot be seen then the patient is a grade III or IV and if, in addition, they have a short thyromental distance, intubation may be 'difficult'.

These two simple bedside tests can be performed at the routine pre-operative visit; any patient identified as having both a grade III or IV view of the pharynx and a thyromental distance of 7 cm or less can be expected to present difficulty with tracheal intubation. In this group of patients, advanced planning of the anaesthetic is mandatory, so that the presence of experienced personnel can be guaranteed. If local analgesic techniques are unsuitable, or if general anaesthesia is essential, the use of an awake intubation technique may be indicated.

Acknowledgments

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Low-flow anaesthesia

Practice, cost implications and acceptability

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Summary

An 8-week survey was conducted to determine whether the introduction of low-flow anaesthesia (a fresh gas flow of 4 litres/minute or less) into routine use would be acceptable to members of a representative anaesthetic department and if the consequent reduction in use of volatile anaesthetics would result in financial savings. The hourly consumption of the volatile agents was measured during anaesthesia conducted using either conventional or low fresh gas flows. Anaesthetists' acceptance of low-flow anaesthesia was assessed using a questionnaire. Data were gathered on 286 patients undergoing inhalational anaesthesia for routine operative procedures. A 54.7% reduction in the consumption of isoflurane and a 55.9% reduction in that of enflurane was found. Of the 28 anaesthetists at the hospital, 21 would use low-flow anaesthesia routinely. The routine use of low-flow anaesthesia would therefore be acceptable and could result in annual savings of £26 870 at Northwick Park Hospital.

Key words

Anaesthetics, volatile; enflurane, isoflurane.
Costs.
Equipment, breathing systems; closed.

Fresh gas flows of 6–8 litres/minute are used in conventional anaesthesia in the United Kingdom, yet lower flows are used routinely in other countries. An anaesthetised patient uses only approximately 10% of this fresh gas.[1] The quantity of volatile anaesthetic agent used is directly proportional to the fresh gas flow into the breathing system, therefore up to 90% of the administered dose of the volatile anaesthetic, typically isoflurane and enflurane, escapes unused into the operating theatre. In low-flow anaesthesia expired gas is recycled and this permits a reduction in the fresh gas flow. Low-flow anaesthesia has been shown to reduce the use of both volatile anaesthetics and of nitrous oxide in strictly defined circumstances.[2–4] These studies do not address the question of the acceptability of low-flow anaesthesia, nor can the savings shown be extrapolated to apply in ordinary anaesthetic departments because these studies were carried out by low-flow enthusiasts using fresh gas flows as low as 0.5 litre/minute. In routine practice low-flow anaesthesia cannot be continuously employed for the whole duration of the anaesthetic and an unspecified period of high fresh gas flow is necessary in the early part of the anaesthetic. This makes prediction of savings difficult. This study examined anaesthetists' attitudes towards low-flow anaesthesia and quantified the monetary savings which could be achieved in routine practice by the members of a representative anaesthetic department.[5]

Methods

Patients

All surgical patients receiving inhalational anaesthesia using nitrous oxide and either enflurane or isoflurane were eligible for inclusion. Children less than 5 years of age and patients undergoing ear, nose and throat surgery were not studied.

Anaesthetic techniques and equipment

Induction of anaesthesia was carried out in the anaesthetic rooms using either thiopentone sodium (Intraval Sodium, May and Baker) 5–7 mg/kg or propofol (Diprivan, ICI)

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2–2.5 mg/kg administered intravenously. Anaesthesia was continued throughout using a mixture of oxygen, nitrous oxide and either enflurane (Enflurane, Abbott) or isoflurane (Forane, Abbott) delivered by Ohmeda Tec 3 and Tec 4 continuous flow vaporizers (Ohmeda, BOC Health Care, West Yorkshire, UK). In the operating theatre this was delivered by adapted Cavendish 750 anaesthetic machines (Medical and Industrial Equipment (M&IE), Exeter, UK). In all anaesthetic rooms anaesthesia was administered using conventional fresh gas flows (approximately 6–8 litres/minute) to permit rapid achievement of the desired level of anaesthesia. Spontaneously breathing patients received inhalational anaesthesia via a Magill breathing system (Medical and Industrial Equipment, Exeter, UK). Patients who required mechanical ventilation had tracheal intubation and intermittent positive pressure ventilation (IPPV) using Manley MP3 ventilators (Blease Medical Equipment Ltd, UK). After induction, patients were transferred to the operating theatre. In two operating theatres patients were maintained under anaesthesia using either Magill breathing systems or Manley MP3 ventilators with conventional high fresh gas flows. In two other operating theatres, patients were maintained using low fresh gas flows of 4 litres/minute or less, administered via an M & IE circle system which incorporated a Jumbo 90 Circle Absorber containing Durasorb (self-indicating soda lime) as a carbon dioxide absorber on its expiratory limb (Medical and Industrial Equipment, Exeter, UK). Patients in the low-flow group requiring IPPV were ventilated using oxygen-driven Penlon Nuffield Series 200 ventilators (Penlon Ltd, Oxon, UK) connected to the circle system.[6] Intavent laryngeal masks (Colgate Medical Ltd, Berks, UK) were inserted in spontaneously breathing patients in the low-flow group to maintain a leak-free breathing system.[7]

All patients were monitored using Cardiocap CC-104 monitors (Datex Instrumentation Corporation, Helsinki, Finland). This included the monitoring of blood pressure, heart rate, inspiratory oxygen and nitrous oxide tensions, end-expiratory carbon dioxide tensions and arterial oxygen saturation. Peak inspiratory and end-expiratory concentrations of enflurane and isoflurane were also measured in patients in the low-flow group using Lamtec 605 Agent Monitors[8] (Lamtec Medical Equipment Ltd, Stevenage, UK) and continuously displayed using peak and trough meters (designed by M. Rosenthal, Bioengineering Department, Clinical Research Centre, Harrow, UK) connected to the external analogue output of the Lamtec meters. A Wright Mark 8 respirometer (Medical and Industrial Equipment, Exeter, UK) incorporated in the circle system measured tidal volume.

Data collection methods

All 28 anaesthetists in the department agreed to take part in the study. Each anaesthetist used low-flow anaesthesia on patients on at least one surgical list and conventional anaesthesia on patients on the same number of surgical lists. The duration of anaesthesia, the administered concentration of volatile anaesthetic, the fresh gas flow rate and the volume of liquid volatile anaesthetic used in the anaesthetic room and in the operating theatre were measured for each anaesthetist for each surgical list and the consumption of volatile anaesthetic was calculated for conventional and low-flow anaesthesia.

At the end of the study anaesthetists attitudes towards low-flow anaesthesia were examined by a questionnaire.

Statistical methods

A split-unit analysis of variance was carried out on the consumption figures for isoflurane and enflurane. Lists were paired according to the most senior anaesthetist conducting anaesthesia for the list, therefore the statistical analysis was based on 13 pairs of lists from 13 senior anaesthetists although 26 anaesthetists actually provided data for the study. The comparison of high- and low-flow techniques was based on the variability between lists within pairs while the comparison of anaesthetic room and operating theatre sites and the interaction between technique and site were based on the variability within lists. Consumption of volatile agents and the variability in fresh gas flows at each site, in both techniques, were expressed as means and their 95% confidence intervals based on the pooled estimate of variability from the analysis of variance.

Ethics

The Chairman of the Ethics Committee at Northwick Park Hospital advised that Ethics Committee approval was not required for this study, since low-flow anaesthesia is a standard anaesthetic technique.

Results

Reduction in consumption of anaesthetic

Data, which represented 321 hours of anaesthesia, were collected on 286 patients, (46 sessions for isoflurane and 52 sessions for enflurane). The results for isoflurane are shown in Table 1 and those for enflurane in Table 2, presented as means with the 95% confidence intervals shown in

Table 1. Total hours of anaesthesia and sessional consumption of isoflurane and sessional fresh gas flow rates shown as mean (95% confidence interval).

	Anaesthetic room		Operating theatre	
Measurement	Low-flow group	High-flow group	Low-flow group	High-flow group
Total hours of anaesthesia	10.3	7.7	79.0	52.6
Mean fresh gas flow; litres/minute	6.9 (6.6–7.3)	7.0 (6.3–7.7)	2.7 (2.4–3.0)	6.4 (6.0–6.8)
Mean consumption; ml/hour	38.6 (33.1–44.1)	44.2 (38.7–49.7)	9.4 (3.9–14.9)	27.9 (22.4–33.4)

Table 2. Total hours of anaesthesia and sessional consumption of enflurane and sessional fresh gas flow rates shown as mean (95% confidence interval).

Measurement	Anaesthetic room		Operating theatre	
	Low-flow group	High-flow group	Low-flow group	High-flow group
Total hours of anaesthesia	11.2	9.9	93.6	56.0
Mean fresh gas flow; litres/minute	7.1 (6.4–7.7)	7.8 (7.3–8.2)	2.8 (2.5–3.1)	6.7 (6.3–7.1)
Mean consumption; ml/hour	40.6 (34.0–47.3)	60.3 (53.6–66.9)	10.2 (3.6–16.9)	32.3 (25.7–38.9)

brackets. On average, 12.5% of the total anaesthetic time was spent in the anaesthetic room where high flows were always used and the remaining 87.5% in the operating theatre. The mean fresh gas flow for the sessions decreased to less than 3 litres/minute in the operating theatre in both low-flow groups.

Significant differences in consumption between the high- and low-flow technique ($p < 0.001$) and between the anaesthetic room and operating theatre ($p < 0.001$) occurred for both isoflurane and enflurane. The interaction between site and technique was statistically significant for isoflurane ($p = 0.022$) but, unexpectedly, not for enflurane ($p = 0.716$). The mean consumption figure in the anaesthetic rooms for enflurane (but not isoflurane) in the high-flow group greatly exceeded that in the low-flow group, possibly because there was a predominance of patients receiving IPPV in the low-flow enflurane group (57% in the low-flow group, 35% in the high-flow group) whereas the proportion of ventilated and spontaneously breathing patients were approximately equal in the low- and high-flow isoflurane groups.

The overall reduction in the hourly costs of isoflurane and enflurane as a result of the use of low-flow anaesthesia were calculated and are shown in Figure 1. The use of low-flow anaesthesia reduced the hourly cost of isoflurane by 54.7% and that of enflurane by 55.9%. In addition the overall fresh gas flow rate was reduced by 50.9% in the isoflurane groups and 52.5% in the enflurane group.

Acceptability of low flow anaesthesia

Replies were received from all anaesthetists in the department. Ninety-six per cent of the anaesthetists found low-

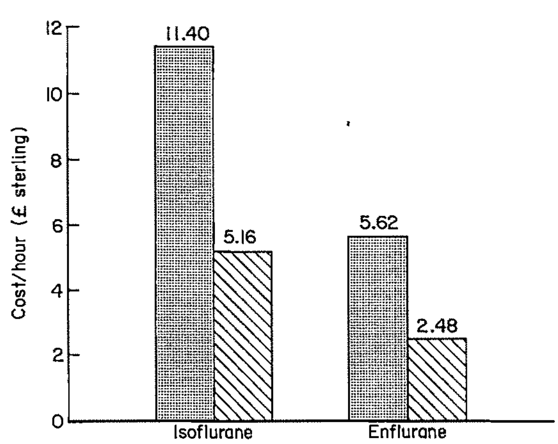

Fig. 1. The hourly cost of isoflurane and enflurane in high (▨) and low (▧) flow anaesthesia shown in pounds sterling.

flow anaesthesia satisfactory and 68% regarded the low-flow circle system as safe and easy to use. Conventional (high-flow) anaesthesia was found easier to use than low-flow anaesthesia by 61% of respondents. However, the majority of anaesthetists indicated that they would use low-flow anaesthesia routinely and only five out of the 28 anaesthetists expressed themselves 'unhappy' at this suggestion. Nineteen anaesthetists considered that it was essential to monitor volatile anaesthetic concentrations in the circle system.

Discussion

Low-flow anaesthesia offers several attractive advantages when compared with conventional anaesthetic techniques. Less anaesthetic gas is vented into the operating theatre thereby decreasing wastage, environmental pollution and any possible risks to the health of staff working in theatres.[9] This study demonstrated the acceptability of low-flow anaesthesia and significant cost savings; the overall hourly cost of isoflurane was reduced by £6.24 and that of enflurane by £3.14.

Previous studies contained small numbers of patients,[2,4] either ventilated[4] or spontaneously breathing,[2] undergoing a narrow range of surgical procedures.[3] Some were carried out by anaesthetists proficient in low-flow anaesthesia who used much lower fresh gas flows than would be employed by the less experienced.[2,4] None had assessed the acceptability of low-flow anaesthesia.[2,4] In contrast, this study was carried out in a representative anaesthetic department on a large number of patients, both ventilated and spontaneously breathing, who received anaesthesia for a wide variety of surgical procedures. The consumption of volatile anaesthetic was also measured during the initial period when high fresh gas flows must be used. The results which we obtained can be extrapolated to routine anaesthetic practice and suggest that the majority of anaesthetists would find low-flow anaesthesia acceptable.

The calculation of the potential annual savings as a result of the routine use of low-flow anaesthesia is complicated by several factors. New equipment, such as ventilators, circle systems, carbon dioxide absorbers and, in the interests of patient safety anaesthetic agent monitors, must be purchased. The cost of equipping a typical operating theatre in this manner was calculated at £5600. Certain patients are unsuitable for low-flow anaesthesia because of the difficulty in maintaining a leak-free breathing system. The advent of the laryngeal mask has solved this problem in spontaneously breathing patients[7] but children less than 5 years old and many ear, nose and throat patients remain unsuitable candidates for low-flow techniques. At

$$T = \frac{£5,600}{NPH}$$

T = Time to recover the cost of new equipment (weeks).

N = The anaesthetic saving factor:
£6.41 for isoflurane
£3.31 for enflurane.

P = The proportion of patients suitable for low flow anaesthesia.

H = The total number of hours of anaesthesia carried out each week in the theatre.

Fig. 2. Estimation of the time taken (in weeks) to recover the expense incurred in equipping one theatre for low flow anaesthesia.

Northwick Park Hospital it was estimated that 92% of patients anaesthetised using either isoflurane or enflurane would be suitable for low-flow anaesthesia.

The introduction of low-flow anaesthesia into routine use at Northwick Park Hospital (where some equipment for low-flow anaesthesia already exists) would reduce the expenditure on enflurane and isoflurane by £25 480 per annum, although the savings in the first year would be reduced to £10 490 because of the initial capital expenditure on new equipment (£14 990). The annual cost of the carbon dioxide absorber (Durasorb), £1020, would be more than offset by the £2410 annual saving on nitrous oxide costs. These estimates of annual savings do not include either the costs of servicing the new equipment and of training staff in its use, or the savings made on oxygen costs, because reliable estimates of these figures were unavailable.

Clinical directors may wish to calculate the financial benefits of low-flow anaesthesia in their hospitals.

The equation in Figure 2 represents an estimate of the time taken (in weeks) to recover the cost of new equipment. The denominator in the equation gives an indication of the likely weekly savings thereafter. The net hourly saving on the cost of isoflurane was calculated as £6.41 and that on enflurane as £3.31, when the saving on nitrous oxide costs and the expenditure on Durasorb are taken into account. If the low-flow anaesthetic technique were routinely used, and when the cost of new equipment has been recouped, an anaesthetic department could expect to save a considerable sum of money annually on volatile anaesthetic agents. As anaesthetists become more familiar with low-flow techniques and further reduce the fresh gas flow, the savings will increase. The use of low-flow anaesthesia may also permit more frequent use of the expensive anaesthetic gas, xenon, and new probably expensive, volatile anaesthetics such as desflurane. This anaesthetic technique offers a means of reducing expenditure without reducing patient care; indeed it could be argued that patient care is increased as a result of the increased monitoring which they receive. Finally, safety considerations with circle systems do not differ in principle from those used with all other systems. Since circle systems contain more connections then the routinely used systems, a case can be made for the use of disconnection alarms, in addition to the monitoring described above.

Acknowledgments

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The effect of intravenous clonidine on the forearm circulation

U. A. CARABINE, P. M. C. WRIGHT, E. KEARNEY, J. P. HOWE AND J. MOORE

Summary

The effect of two doses of clonidine on forearm blood flow was compared with an inert treatment using mercury strain gauge venous occlusive plethysmography. In the clonidine treated groups, forearm blood flow was unaffected in the resting state, but decreased sharply with tracheal intubation. In the saline group, blood flow increased with intubation. Forearm vascular resistance increased in the clonidine treated groups, but decreased in the saline group. These results suggest that clonidine has a peripheral action in anaesthetised normotensive individuals, and is not a purely centrally acting drug.

Key words

Measurement techniques; venous occlusive plethysmography.
Pharmacology; clonidine.

Clonidine is a centrally acting $alpha_2$ adrenergic agonist used mainly for its antihypertensive properties.[1] Its mechanism of action is still uncertain, although it is probably the result of stimulation of central $alpha_2$ adrenergic receptors in the nucleus reticularis lateralis area of the medulla.[2] This results in decreased central sympathetic outflow, and a reduction in blood pressure and heart rate.[3] Clonidine is not thought to have a major effect on the peripheral circulatory system, although with long-term treatment total peripheral resistance may decrease.[4] Recently it has been suggested that clonidine may be of benefit in the peri-operative period, by attenuating episodic hypertension and tachycardia.[5]

The effects of clonidine on the cardiovascular system during anaesthesia are still unclear, so this study compared the reaction of clonidine and a placebo on forearm blood flow and forearm vascular resistance during induction of anaesthesia and tracheal intubation.

Methods

Ethics committee approval and informed patient consent were obtained from 30 healthy patients, scheduled for surgery requiring tracheal anaesthesia.

In a randomised double-blind study patients were allocated to one of three equal groups: group A received clonidine 1.25 μg/kg, group B clonidine 0.625 μg/kg and group C an equivalent volume of 0·9% saline. The test drug was administered intravenously 15 minutes before the induction of anaesthesia. Anaesthesia was induced using thiopentone 3–5 mg/kg and muscle relaxation was achieved with suxamethonium 1.5 mg/kg. The trachea was intubated and the lungs ventilated to maintain normocapnia. Anaesthesia was maintained with nitrous oxide 66% in oxygen, and isoflurane 1% until the end of the 5 minute study period.

The ECG was displayed continuously: heart rate (beats/minute) and mean arterial pressure (mmHg) were measured at 30 second intervals throughout the study period using an automated oscillotonometer. Forearm blood flow (ml blood per 100 ml forearm tissue/minute) and forearm vascular resistance (mean arterial pressure/forearm blood flow, R units) were also recorded at 30 second intervals. Measurements were started 3 minutes before administration of the test drug and continued until 5 minutes after tracheal intubation. The plethysmographic measurements were made by a technician using a standard technique employed in a previous study,[6] who was blind to the treatment given. The baseline values for heart rate, mean arterial pressure, forearm blood flow and forearm vascular resistance were those obtained immediately before test drug administration.

Results are presented as mean (SEM) and were analysed using ANOVA and one way factor analysis. $p < 0.05$ was taken as statistically significant.

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Table 1. Demographic data and baseline circulatory parameters. Values are expressed as mean (SEM).

	Groups		
	A	B	C
Age; years	34 (3)	35 (4)	38 (3)
Weight; kg	68 (3)	65 (3)	61 (4)
Heart rate; beats per minute	76 (5)	66 (3)	73 (3)
Mean arterial pressure; mmHg	94 (4)	90 (4)	92 (3)
Forearm blood flow; ml blood per 100 ml forearm tissue/minute	3.0 (0.5)	3.4 (0.5)	2.9 (0.5)
Forearm vascular resistance: R units	38 (6)	35 (7)	41 (7)

Results

The groups were comparable in terms of age and weight (Table 1). There was no difference in heart rate, mean arterial presure, forearm vascular resistance or forearm blood flow within or among the three treatment groups before administration of the test drug and during the 15 minute pre-induction period (Table 1). Compared to baseline values, the mean arterial pressure was lowest in group A (83 mmHg) immediately before induction of anaesthesia, but this was not statistically significant. Heart rate and mean arterial pressure increased in all groups following tracheal intubation (mean (SEM): group A = 109 (3.4) mmHg, B = 114 (5) mmHg, C = 120 (5) mmHg) and although the increase was lower in the treated than the untreated patients, the difference did not achieve statistical significance ($p < 0.06$). In all three groups, both variables had returned to baseline levels within 3 minutes of induction.

At intubation, forearm blood flow increased in group C but decreased in both clonidine groups (on between-group analysis $p < 0.01$). There was no significant difference between groups A and B (Table 2). At tracheal intubation, forearm vascular resistance decreased slightly in group C and returned to baseline values within 1 minute. Forearm vascular resistance increased at tracheal intubation in groups A and B and regained baseline values within 2 minutes. The difference between group C and both clonidine groups was significant ($p < 0.05$), and the increase in forearm vascular resistance was greater in group A than group B ($p < 0.05$) (Table 2).

Discussion

It has been suggested that the administration of clonidine during the peri-operative period can stabilize cardiovascular dynamics, by preventing undesirable increases in blood pressure and heart rate.[7] Previous work by the present authors[8] indicates some protective effect from clonidine by attenuating the pressor response associated with tracheal intubation.[9] There is no previous work on the effect of acute clonidine administration on the peripheral circulation during anaesthesia.

This study has examined the effects of clonidine on forearm circulation before and after induction of anaesthesia and tracheal intubation. The doses employed are low, bearing in mind that the bioavailability of the drug reaches 100%;[10] the aim was to reduce intra-operative hypotension.[11] The circulatory changes at intubation in untreated healthy subjects are as expected: a substantial pressor response accompanied by an equally substantial increase in forearm blood flow. This reflects the fact that mean arterial pressure is the principal determinant of limb blood flow. Therefore, forearm vascular resistance, the ratio of the two, remains unchanged.

Table 2. Changes in forearm blood flow (ml of blood per 100 ml forearm tissue/minute) and forearm vascular resistance (R units) before and after test drug administration. Values are expressed as mean (SEM).

	Forearm blood flow		
	A	B	C
Baseline	3.0 (0.5)	3.4 (0.6)	2.9 (0.5)
Induction	4.9 (1.1)	5.9 (0.9)	5.2 (1.0)
Intubation	2.5 (0.5)*	2.9 (0.5)*	5.4 (1.1)
Intubation+1	2.9 (0.5)*	4.2 (0.9)	4.7 (1.0)
Intubation+3	4.5 (0.8)	3.8 (1.0)	3.7 (1.0)
Intubation+5	4.2 (0.8)	3.6 (0.6)	3.9 (0.8)
	Forearm vascular resistance		
	A	B	C
Baseline	38.4 (6)	34.9 (7)	40.5 (7)
Induction	22.4 (3)	16.9 (3)	36.9 (2)
Intubation	65.5 (16)*/**	49.4 (8)*	30.5 (6)
Intubation+1	56.1 (15)*	40.5 (9)	37.3 (8)
Intubation+3	31.1 (8)	40.3 (9)	42.3 (8)
Intubation+5	30.3 (7)	34.2 (6)	35.0 (6)

* $p < 0.05\%$ compared to control.
** $p < 0.05\%$ compared to low dose clonidine.

The circulatory changes at intubation associated with clonidine administration are different and more complex. The pressor response remains largely intact, but the expected increase in limb blood flow is not only absent, but reversed. The forearm vascular resistance changes are also very different in that there is a marked increase with clonidine compared to no change in the untreated patients. Further, there is some indication that these effects are dose related.

There are a number of possible explanations for these findings. Although the main peripheral effect of clonidine is presynaptic, it is only a partial agonist and is also known to exhibit postsynaptic $alpha_2$ agonist activity in the peripheral circulation.[12] This postsynaptic action is vasoconstrictor and can explain the transient hypertension immediately following rapid intravenous administration.[13] This effect is only significant at high plasma concentrations and has not been reported after a 15 minute time lapse, nor has it been studied in the context of the sort of haemodynamic challenge that accompanies tracheal intubation. In addition, clonidine may also possess $alpha_1$ agonist activity in the peripheral circulation, and this is predominantly vasoconstrictor.[14] There is some evidence for a therapeutic window effect, that is very high or very low doses of the drug can alter the expected cardiovascular response to the drug.[15] At low doses, this may be due to a plasma concentration that is inadequate to produce a therapeutic effect. The explanation at the other extreme may be more complex, but there is a suggestion that at higher doses, stimulation of central $alpha_1$ adrenoceptors may functionally antagonise an $alpha_2$ mediated effect. This post receptor 'cross talk' has been noted with more specific $alpha_2$ adrenergic agonists, and may explain an unexpected cardiovascular response.[16]

In conclusion, clonidine can affect both peripheral and central circulatory mechanisms, and although it may be of some potential benefit in peri-operative management, the vascular effects of this complex drug require further study before its use can be advocated for routine use.

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Gastric emptying following Caesarean section and the effect of epidural fentanyl

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Summary

The rate of absorption of paracetamol following oral administration was used as an indirect measure of the rate of gastric emptying. This was to determine the effect on gastric motility of the addition of fentanyl to a solution of local anaesthetic given into the epidural space to provide pain relief following Caesarean section. Thirty subjects were randomly allocated to receive either bupivacaine plus fentanyl or bupivacaine alone. The area under the curve of the graph of plasma paracetamol concentration versus time was calculated for each subject at 45 and 90 minutes after administration of the epidural injection, and this value was used as an index of the rate of gastric emptying. This study demonstrated that gastric emptying may be normal immediately following Caesarean section under epidural anaesthesia, but that if fentanyl is added to the epidural solution, gastric emptying is significantly slower in the first 45 minutes following surgery ($p < 0.05$).

Key words

Gastrointestinal tract: stomach, volume.
Analgesics; fentanyl.
Anaesthetic techniques, regional; epidural.
Anaesthesia; obstetric.

Opioids injected into the cerebrospinal fluid or epidural space have proved useful in providing pain relief in a variety of clinical situations. However, the side effects observed are qualitatively similar to those seen when the drugs are given by traditional parenteral routes. The slowing of gastric emptying associated with intramuscular administration of opioids is well recognised,[1,2] but little is known about gastric emptying following the administration of opioids into the epidural space. Epidural fentanyl is widely used in obstetric anaesthetic practice to provide analgesia in labour, particularly for the relief of rectal pressure, and also during and following Caesarean section. In this study the effect on gastric motility of adding fentanyl to a solution of local anaesthetic given into the epidural space following Caesarean section was assessed using the rate of absorption of orally administered paracetamol as an index of the rate of gastric emptying.[3]

Methods

Mothers scheduled to undergo elective Caesarean section at 36+ weeks' gestation with a singleton pregnancy were studied. Those with a history of renal, hepatic or gastrointestinal disease or who had received opioids or paracetamol within the previous 24 hours were not studied. The study was approved by the Hospital Ethics Committee and informed consent was obtained from each subject.

Each mother received ranitidine 150 mg given orally on the previous evening and repeated on the morning of surgery. Epidural block for Caesarean section was established using 0.5% bupivacaine, and at the end of surgery the mothers were randomly allocated to one of two groups. Group A received an epidural injection of 8 ml bupivacaine 0.25% plus 2 ml 0.9% saline and group **B** received 8 ml bupivacaine 0.25% plus 2 ml fentanyl (50 μg/ml) by the same route. At this time all subjects were given, by mouth, 1.5 g of soluble paracetamol dissolved in 50 ml of water. Blood was withdrawn through an indwelling venous cannula just before administration of the test solution and at 15 minute intervals thereafter for 90 minutes. These samples were subsequently analysed to determine plasma paracetamol concentration using an assay kit obtained from Cambridge Life Sciences plc. The method involves the degradation of acetaminophen by the bacterial enzyme aryl acyclamide aminohydrolase. The products of reaction are acetate and p-aminophenol and the latter reacts with

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Table 1. Demographic data of patients in both groups. Values expressed as median (range).

	Group A	Group B
Maternal age; years	28 (23–40)	30 (22–37)
Gestational age; weeks	40 (37–41)	40 (37–42)
Maternal weight; kg	77 (57–91)	70 (65–89)

o-cresol and ammoniacal copper sulphate to produce a compound which is detected colorimetrically. In our laboratory, the lower limit of accurate detection is 3 mg/litre and the coefficient of variation for replicate analyses (precision) at 10 mg/litre is 5%. When this method is compared with gas-liquid chromatography and spectrophotometric analysis the correlation coefficients have been found to be 0.98 and 0.99 respectively.[4] The analysis was performed by a technician who was unaware of the solution administered.

Recordings of arterial blood pressure, heart rate and respiratory rate were made at 30 minute intervals throughout the study period.

Statistical methods

Analysis of the serial measurements of plasma paracetamol concentration was carried out in accordance with the guidelines of Matthews and his co-authors.[5] The area under the curve of the graph of plasma paracetamol concentration against time was calculated for each subject for the first 45 minutes and the entire 90 minutes of the study. These values were taken as summary measures of the rate of gastric emptying. Comparison of the serial data for the test groups was carried out using the Wilcoxon Rank-Sum test.

Results

Thirty women aged 22–40 years, and at 37–42 weeks' gestation, completed the study. The groups were comparable with respect to maternal age, gestational age and maternal body weight (Table 1).

A wide variation in the extent of gastric emptying at 45 and 90 minutes was observed in both groups. This was

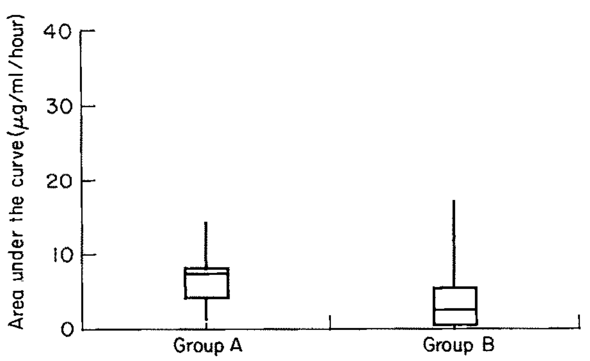

Figure 1. Values of AUC in the plasma paracetamol concentration versus time graph at 45 minutes following administration of paracetamol for group A (bupivacaine only) and for group B (bupivacaine plus fentanyl). The ends of the vertical lines are the limits of the range, the uppermost and lowest horizontal lines are the limits of the interquartile range, and the intermediate horizontal line is the median value.

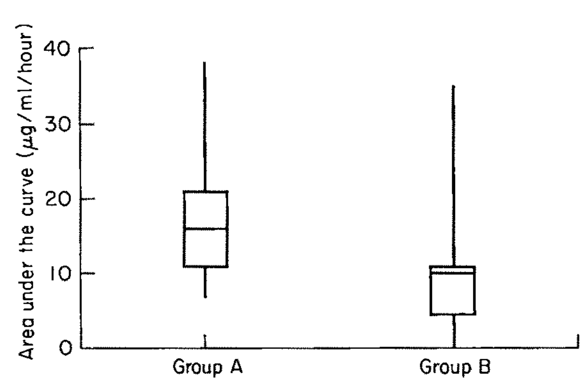

Figure 2. Values of AUC in the plasma paracetamol concentration versus time graph at 90 minutes following administration of paracetamol for groups A and B. The form of the display is as in Figure 1.

particularly apparent in the group who received epidural bupivacaine plus fentanyl. The distribution of values for the area under the curve (AUC) for group A (bupivacaine only) and for group B (bupivacaine plus fentanyl) at 45 minutes is shown in Figure 1. The median value (interquartile range (IQR)) for group A was 7.5 μg/ml/hour (4.3–8.0) and for group B 2.5 μg/ml/hour (0.4–5.6). Four women in group B had no gastric emptying in the first 45 minutes, whereas all women in group A had some gastric emptying. When the values of AUC for the two groups were compared using the Wilcoxon Rank-Sum test the difference was found to be significant ($p < 0.05$).

Figure 2 shows the values of AUC for the entire 90 minutes. The median value (IQR) for group A was 16.1 μg/ml/hour (10.9–21.1) and for group B 9.9 μg/ml/hour (4.5–10.9). The difference between the two groups was not significant. Two mothers who received fentanyl had no gastric emptying for the entire 90 minutes.

Figures 3 and 4 show the peak plasma paracetamol concentration plotted against the time after administration at which it occurred for the two groups. Two subjects in group B had no measurable paracetamol concentration at any time during the 90 minutes and so this figure shows only 13 data points. Peak concentrations occurred earlier in group A with 10 out of 15 subjects having peak concentration in the first 45 minutes, compared with only six out of 15 in group B. This difference was not significant (Chi-square test).

One mother in group A had a short-lived episode of

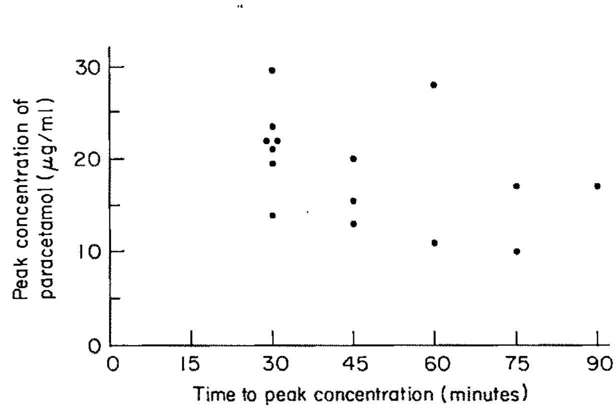

Figure 3. Peak plasma concentration of paracetamol versus the time after administration at which it occurred in group A.

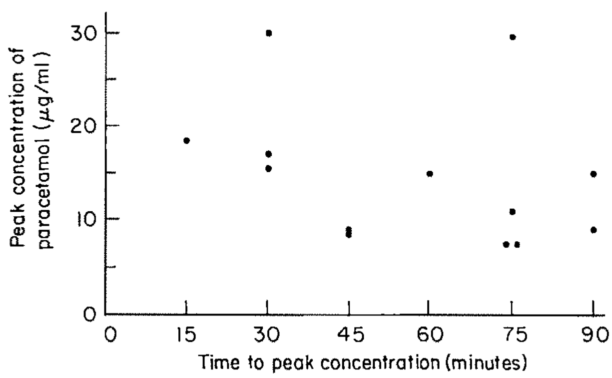

Figure 4. Peak plasma concentration of paracetamol versus the time after administration at which it occurred in group B. (Only 13 points are shown as two subjects had no gastric emptying during the trial period.)

hypotension 30 minutes after administration of the epidural solution. There were no requests for analgesia in either group during the 90 minutes of the trial.

Discussion

Gastric emptying in the group who received epidural bupivacaine and fentanyl was slower than in those who received bupivacaine alone. Comparisons of the extent of gastric emptying were made at 45 and at 90 minutes following the epidural injection and the difference was found to be significant for the first 45 minutes only. In addition, there was a tendency for peak concentrations of paracetamol to occur earlier in the group who received bupivacaine only, but this difference was not significant. There were no differences between the groups with respect to intra-operative or postoperative course that might have contributed to these effects. It was observed that there were subjects who had normal gastric emptying and subjects with slow gastric emptying immediately following surgery in both groups..

There was a much greater variation in the rate of gastric emptying in the group who received fentanyl than reported in subjects receiving intramuscular opioids before elective general surgery.[1] Plasma fentanyl concentration following epidural administration has been reported as varying from below the minimum detectable level to a level which would produce systemic analgesia following thoracic surgery and Caesarean section.[6] The disposition of fentanyl following epidural administration would appear to be unpredictable in clinical practice, although a theoretical model giving the relative contributions of transfer across the dura and absorption into the epidural veins has been described.[7] These authors suggested that increased flow in the epidural venous plexus during pregnancy could increase the proportion of drug entering the systemic circulation, and so one might expect the subjects in this study to have relatively high plasma concentrations of fentanyl.

It is possible that the effect demonstrated is simply due to extensive absorption of fentanyl into the epidural veins resulting in high systemic levels in the subjects with delayed gastric emptying and minimal absorption in the others. However, the authors who described delayed gastric emptying following administration of morphine into the thoracic epidural space[8] found that the delay occurred in the presence of plasma morphine concentrations lower than those seen following intramuscular administration of morphine to the same subjects. They speculated that delayed gastric emptying resulted from the drug that reached receptors in the central nervous system influencing gastric motility by distribution from the cerebrospinal fluid rather than the systemic circulation; hence the effect was thought to be independent of the systemic concentration of the opiate.

In the present study 10 of the 15 mothers who received epidural bupivacaine alone had a peak paracetamol concentration in the first 45 minutes, and so had a normal rate of gastric emptying.

Similarly, patients having epidural analgesia following hysterectomy[9] displayed rates of gastric emptying which were not significantly different from a control group. The use of epidural analgesia avoids or blocks some of the factors producing a delay in postoperative gastric emptying. Such factors include pain, opioid analgesics and increased sympathetic nervous system activity.

In conclusion, there is evidence that fentanyl given into the epidural space can cause a delay in gastric emptying. This should be borne in mind if further surgery is required in the early postoperative period.

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Stressful pre-operative preparation procedures

The routine removal of dentures during pre-operative preparation contributes to pre-operative distress

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Summary

One hundred and twenty-four patients (76 women and 48 men) were interviewed within the first 36 hours after operation. Fifty per cent of those studied were denture wearers. They were asked to fill in a questionnaire which registered their levels of distress about the various pre-operative preparation procedures. The most common factors contributing to pre-operative distress were waiting for transfer to the operating theatre, the prohibition of fluids and the removal of dentures.

Key words

Complications; pre-operative anxiety.
Dentures.

Anxiety is commonly experienced by patients awaiting surgery. Wide variations in the degree of anxiety exist. These are influenced by many factors including the basic (premorbid) personality, the type of operation, age and previous experience of anaesthesia. The sex of the patient does not influence the overall degree of anxiety.[1]

Anxiety not only causes psychic disturbance but may also contribute to problems during anaesthesia. Raised pre- and intra-operative plasma adrenaline levels have been measured in patients who exhibit pre-operative anxiety. This may cause unwanted pharmacokinetic interactions with anaesthetic induction agents.[2] Cardiac arrhythmias at times of stress have also been noted.[3] The pre-operative visit,[1,4] the use of anxiolytics, in the form of benzodiazepines, and beta-adrenergic blockers[5] have been found to diminish pre-operative anxiety.

Anxiety, being an emotion, is difficult to measure objectively. There are two broad approaches which can be adopted. Firstly, the degree of anxiety can be measured using a standardised scale such as Speilberger's State-Trait Anxiety Inventory.[6] This has been used to demonstrate the heightened levels of anxiety experienced by surgical patients.[7,8] An alternative approach involves assessing the individual's perception of the stressors which cause, or contribute to, that anxiety. Examples of this technique are the Hospital Stress Rating Scale[9] and the Patients' Opinion Form.[10] There have been few studies which examine specific stressors for surgical patients[11] or which explore the patient's response to preparation for theatre.

The purpose of this study was to determine which events patients found distressing during routine pre-operative preparation, with particular reference to the removal of dentures.

Method

Ethical approval for the study was obtained from the Joint Ethics Committee of South Glamorgan Health Authority and the University of Wales College of Medicine. Patients who had undergone a surgical procedure in the previous 36 hours were invited to fill in a questionnaire anonymously. The questionnaire was administered by one of the investigators. Patients who had had emergency surgery, who were mentally ill, who were assessed by the anaesthetist as ASA grades 3–5, or who were admitted to the high dependency or intensive therapy units postoperatively were not studied.

Patients were asked to respond to 16 different questions about pre-operative preparation procedures which could be considered stressors. The investigator noted the age, sex, surgical procedure, any premedication that had been given and whether the subject was a denture wearer. In answer to each question the patients ticked one of six responses that most appropriately described their feelings. The options varied from 'didn't worry me at all' to 'unbearable' (Table 1). These responses were given a weighted score (from 0–4). The mean score was taken to represent the overall level of distress for each item. A Chi-squared test was used to assess the association between sex or age group and response using just two categories: those who indicated some level of distress (score 1–4) and those who indicated none (score 0).

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Table 1. Responses to questionnaire (n = 124).

Item Score	0	1	2	3	4	Mean score
1. Not being allowed to eat	103	12	1	2	3	0.26
2. Not being allowed to drink	65	35	10	10	2	0.76
3. Having to wear the gown	112	7	1	3	—	0.15
4. Having to remove my nail varnish	33	—	—	1	—	0.09
5. Having a label over my bed	122	—	—	—	—	0.00
6. Not being allowed to wear my dentures	29	25	3	2	2	0.74
7. Being shaved	25	6	3	—	—	0.35
8. Having my jewellery removed or covered	89	4	—	—	—	0.04
9. Being given the premed	94	4	2	—	1	0.12
10. Waiting to be collected for theatre	56	37	12	7	8	0.95
11. Being taken on the trolley to theatre	90	20	7	3	4	0.48
12. Going inside theatre	87	19	8	6	3	0.53
13. Seeing all those machines	88	17	4	6	—	0.37
14. Being anaesthetised	87	21	6	9	1	0.52
15. Being weighed	91	—	1	—	1	0.07
16. Having my operation site marked	51	5	—	2	—	0.22

0–Doesn't bother me at all; 1–Not very pleasant; 2–Unpleasant; 3–Very unpleasant; 4–Unbearable.
Responses 1–4 were taken to indicate that the item was found disagreeable and could therefore be considered a stressor.

Results

One hundred and twenty-four adults, all in ASA grades 1 or 2, agreed to complete the questionnaire. Only one patient refused to complete it (response rate 99.2%). The sample was composed of 76 women (mean age 54.8 years, SD 18.4), and 48 men (mean age 61.5 years, SD 19.4). Sixty-two patients were denture wearers.

The results are shown in Table 1. Not all patients experienced all of the 16 pre-operative events listed in the questionnaire. 'Not being allowed to wear my dentures' was given the third highest rating of all the items on the list. This was experienced by 61 patients, 32 of whom found this disagreeable (mean score 0.74). Of the two items which scored higher, the highest rating was given to 'waiting to be collected for theatre', which happened to 120 patients, 64 of whom rated this as disagreeable (mean score 0.95). 'Not being allowed to drink', noted by 122 patients, was given the second highest rating, (mean score 0.76), (Table 1).

There was a significant association between the sex of the patients and the response to the removal of the dentures (Table 2). Of the 29 who responded that they were 'not bothered', only 10 were female whilst of the 32 whose responses suggested that they found this disagreeable, 27 were female.

There was also an association between sex and the responses to other items. Women were more likely to rate as disagreeable 'not being allowed to drink', 'going inside theatre' and 'being anaesthetised'.

There was no association between age group (under or over 60 years) and responses to the removal of dentures. However, younger patients were significantly more likely to rate as disagreeable 'not being allowed to eat', 'seeing the machines' and 'being anaesthetised' (Table 3).

Discussion

Nursing staff usually follow a protocol for the preparation of the patient for surgery. In the United Kingdom this includes removal of the patient's dentures. Other countries, for example those of Australasia, commonly allow patients to wear their dentures to the operating theatre. Patients who are to be intubated either remove their dentures themselves immediately prior to induction, or the dentures

Table 2. Items with sex difference.

	Males		Females				
	0	1–4	0	1–4	Chi-squared	df	p
2. Not being allowed to drink	34	13	31	44	9.95	1	0.0016
6. Not being allowed to wear my dentures	19	5	10	27	13.85	1	0.0002
12. Going inside theatre	40	8	47	28	5.08	1	0.0242
14. Being anaesthetised	40	8	47	29	5.50	1	0.0190

Table 3. Items with age group difference.

	Under 60		60+				
	0	1–4	0	1–4	Chi-squared	df	p
1. Not being allowed to eat	42	13	61	5	4.91	1	0.0267
13. Seeing all those machines	31	19	57	8	9.00	1	0.0027
14. Being anaesthetised	30	27	37	10	13.97	1	0.0002

are removed by the anaesthetist after induction but before intubation. The dentures are placed in a labelled container and are reinserted by the patient in the recovery room. Patients receiving anaesthesia by mask leave their dentures *in situ* throughout the anaesthetic.

The reasons given for removing dentures are 'that the anaesthetised patient could swallow them' or that 'they might become dislodged and cause respiratory obstruction'. Although this is a possibility in partial plate wearers, it is unlikely with full set dentures. Many denture wearers sleep comfortably and safely with their dentures *in situ*, removing them only for cleaning. Allowing patients to wear their dentures to the operating theatre affords them greater dignity and may lessen pre-operative distress. Additionally, it overcomes the problem of leakage of gases between the mask and the sunken checks of the edentulous patient.

Therefore, although there are many factors and events associated with the development of pre-operative distress, the removal of dentures, often several hours before surgery, may make it worse.

Previous studies have addressed the nature of pre-operative anxiety.[12] It is well recognised that the pre-operative visit is important to identify and allay patient apprehension.[4] However, this visit can be beneficial only if those features of pre-operative preparation which provoke distress in the patient can be identified.

'Not being allowed to wear my dentures', scored the third highest rating of 'unpleasantness'. There was no association between age and response to the removal of dentures. There was a highly significant difference between males and females; women were significantly more distressed than men at having to remove their dentures, one patient even describing it as 'unbearable'. It is not difficult to appreciate why this is so. Women are generally more concerned with their physical appearance and many female denture wearers have never been seen without their dentures, even by their husbands. The removal of dentures is an act of depersonalisation and is of questionable benefit. The possibility that they may be 'swallowed' or obstruct respiration is extremely remote. Allowing patients to wear their dentures to the operating theatre would markedly reduce distress.

Not surprisingly, 'waiting to be collected for theatre' was rated the most highly distressing pre-operative event. This is in accordance with earlier work by McCleane *et al.*[12] who found that only the fear of pain generated greater pre-operative anxiety. Unfortunately, despite all attempts to give patients an idea of the time they may have to wait before being transferred to the operating theatre, there will always be the possibility of unforeseen delays. Even if it were possible to give an exact transfer time, the level of distress might not be less, the anticipation of the surgery being enough to provoke distress. At present the prescription of anxiolytic drugs as premedicants remains the only available means of addressing this problem.

The second highest distress rating was recorded in response to 'not being allowed to drink'. Goresky and Maltby[13] have shown that gastric fluid pH and volume are independent of the duration of fluid fast greater than 2 hours, provided that only clear fluids are consumed on the day of operation.[14–17] Agarwal *et al.*[18] supported the view that fluid fasting is not justified in elective surgical patients. However, fluid deprivation from midnight is commonplace for morning elective surgical lists, often resulting in a fluid fast of more than 10 hours. Patients on afternoon lists fare only a little better, having their last fluid a minimum of 6 hours pre-operatively. A dry mouth and thirst are not only distressing but are accompanied by dehydration, an unwelcome situation prior to induction of anaesthesia. Work by Goresky and Maltby[13] suggests that long fluid fast is unnecessary. The Canadian Society of Anaesthetists recommends that departments of anaesthesia should formulate a policy about pre-operative fasting.[19]

In addition to the sex differences found in response to the removal of dentures, we also found that females were more likely to be distressed by not being allowed to drink, entering the operating theatre and being anaesthetised. This is in contrast to the work of McCleane[8] and Ramsay[1] which failed to demonstrate a sex difference in the level of pre-operative anxiety.

Although we were unable to demonstrate an association between age and the response to the removal of dentures, this was not so in the responses to other events. Younger patients were significantly more likely to register distress at not being allowed to eat, at seeing the anaesthetic machine and at being anaesthetised. This may be attributable to the older age group having had previous experience of anaesthesia and surgery.

In conclusion, although pre-operative preparation protocols are necessary, it may be that the time has come for departments of anaesthesia to consider a revision of their policies for pre-operative preparation, particularly on the removal of dentures. We suggest that changes are possible which are not only safe for the patient but would also alleviate some pre-operative distress.

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The effect of a priming epidural injection of adrenaline on epidural blockade with bupivacaine

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Summary

Twenty-four patients receiving epidural anaesthesia were studied to test the hypothesis that 1:200 000 adrenaline administered into the epidural space 5 minutes before 20 ml bupivacaine 0.5% would improve nerve block and delay systemic absorption of the local anaesthetic. Group A/B received 20 ml adrenaline 1:200 000 5 minutes before 20 ml bupivacaine 0.5%, group S/BA 20 ml saline followed by 20 ml bupivacaine 0.5% with 100 μg adrenaline, and group S/B saline 20 ml followed by 20 ml plain bupivacaine 0.5%. Mean maximum plasma concentrations of bupivacaine tended to be lower in the adrenaline groups. A delay in the time to peak plasma concentration of bupivacaine was noted in the A/B group; this indicated that priming with adrenaline may be effective at delaying early systemic uptake of the local anaesthetic. In both adrenaline groups a more prolonged epidural block and increased efficacy were noted, although this was only significant for the duration of block at T_6 ($p = 0.023$) and duration of motor block at Bromage level 1 ($p = 0.016$) in group A/B. There seems little clinical advantage in administering adrenaline 5 minutes before bupivacaine.

Key words

Anaesthetic techniques regional; epidural.
Anaesthetics, local; bupivacaine.
Adrenaline.

Bupivacaine is an amide local anaesthetic often used to provide epidural analgesia. It is described as a long-acting agent, but the duration of action is affected significantly by the vascularity of the area into which it is injected.[1,2] Increased vascularity is associated with an increased systemic absorption rate and a decreased duration of neural blockade. Bupivacaine may enhance its own absorption directly by causing vasodilatation and indirectly by sympathetic blockade.[1] Vasoconstrictors are added to injections of local anaesthetic to lower peak plasma concentration and hence reduce the risk of systemic toxicity.[3,4] They may also increase the duration of blockade, the depth of blockade and, in the case of epidural anaesthesia, the extent of the block. The recommended concentration of adrenaline to produce maximum effect with minimum side effects is thought to be 1:200 000.[2,4] In the numerous studies reviewed by Tucker and Mather[2] in 1979, and in a recent study,[5] vasoconstrictors lowered the peak plasma concentrations of local anaesthetic after epidural injection, but did not always prolong the time to peak concentrations. This suggests that significant absorption of the local anaesthetic occurs before the full vasoconstricting effect of adrenaline becomes apparent.[2,3] Some support for this suggestion comes from a recent study on the effect of 1:200 000 adrenaline on the absorption of diamorphine. Priming the epidural space with adrenaline resulted in lower mean plasma diamorphine levels than observed when the adrenaline was given at the same time as the diamorphine.[6] It is also known that adrenaline takes approximately 5 minutes to exert its vasonconstrictor effect.[7] Therefore, we decided to investigate the effect of priming the epidural space with 1:200 000 adrenaline 5 minutes before the injection of bupivacaine. We compared results in the pretreated group with those in a group in whom the adrenaline was given at the same time as the bupivacaine, and with those in a group that was given plain bupivacaine alone.

Methods

Local ethics committee permission was obtained and all patients gave informed written consent. All patients were ASA grades 1 and 2, aged less than 60 years and scheduled

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for routine extracorporeal shock wave lithotripsy. Routine ECGs were performed on all patients, who were allocated randomly into one of three groups; the study was performed in a double-blind manner. The treatment protocols were assigned by choice of sealed envelopes and both protocol and drug were checked by an independent anaesthetist.

No premedication was used. A large bore intravenous cannula was inserted into a vein in each arm. One was used to administer an infusion of compound sodium lactate solution, and the other, which was kept patent with heparinised saline, was used to take blood samples. An epidural catheter was inserted using a 16 G Tuohy needle at the L_{2-3} level by the midline approach and loss of resistance to saline method. The catheter was flushed with saline before insertion and introduced to leave 4 cm in the epidural space. Following fixation of the catheter, the patient was returned to the sitting position at approximately 45°.

A continuous ECG monitor was attached to the patient and blood pressure was measured at one minute intervals using an automatic noninvasive technique. One litre of compound sodium lactate solution was infused intravenously before the injections into the epidural space. A 3 ml epidural test dose of 1% plain lignocaine was given, followed 4 minutes later by the priming drug, 20 ml of either saline or 1:200 000 adrenaline in saline, injected over one minute. After a further 5 minutes, 20 ml of bupivacaine, either with adrenaline 1:200 000 or as plain solution, was given over 2 minutes. The end of this injection was taken as time zero.

The three patient groups were designated: S/B = saline prime followed by plain bupivacaine, S/BA = saline prime followed by bupivacaine with 1:200 000 adrenaline, A/B = adrenaline 1:200 000 prime followed by plain bupivacaine.

Over a 2 hour period serial measurements of systolic, diastolic and mean blood pressure, and pulse rate were made. The spread of sensory analgesia, as detected by loss of sensation to the blunt end of a 27 G short dental needle, was recorded at 2, 5, 10, 15, 25, 30 minutes and every 30 minutes thereafter until the block had worn off. Motor blockade (MB) was measured at the same time using a modified Bromage scale. The grades of MB were: 0 = no paralysis, full flexion of knee and feet; 1 = inability to raise extended leg, just able to move knees; 2 = inability to flex knees, can move feet only; 3 = inability to flex ankle joint or any part of leg.

The quality of analgesia was scored from 1–3 (1, no pain; 2, mild discomfort; 3, severe pain). Any concomitant medication or complications were also noted.

Table 1. Demographic data.

	S/B group	S/BA group	A/B group
Mean age years; (SD)	46.4 (13)	50.0 (8.6)	49.9 (11)
Mean weight kg; (SD)	76.1 (15)	85.1 (14)	85.3 (21)
Mean height cm; (SD)	174 (6.4)	175 (7.3)	178 (11)

Statistical analysis

For normally distributed data, multiple group comparisons were performed by the analysis of variance (ANOVA) statistical test. This was followed by the two-sided unpaired Student's *t*-test when indicated. Nonparametric data analysis involved the use of the Kruskal–Wallis test followed by the Mann–Whitney *U* test when indicated. Statistical comparisons of frequency were made with the Chi-squared test (with Yates' continuity correction). Statistical significance was assumed at the 5% level.

Results

The three groups of patients were matched for age, weight and height (Table 1). The S/B and S/BA groups comprised men only, the A/B group included two females. The male bias was due to the nature of the surgery. In each group seven out of the eight patients had satisfactory analgesia, with one patient requiring supplementary analgesia. No patients developed complications.

Figure 1 shows the mean cardiovascular changes associated with the three epidural treatments. Adrenaline caused a mean rise in pulse rate greater than the 95% confidence interval at several time points. However, the highest mean rise in pulse rate at any time within the monitored 2 hour period was not significantly different between groups and the time spent with a relatively raised pulse rate of either 10% or 15% was also not significantly different at the 5% level (Table 2). Systolic, diastolic and mean blood pressure fell in all three groups. The time spent at a systolic blood pressure of either 90% or 75% of the baseline value was not significantly different between the groups; the maximum fall in systolic blood pressure was also not significantly different (Table 2). One patient in each of the groups required ephedrine and atropine, and one patient in each of the S/BA and A/B groups required ephedrine alone. The amount of intravenous fluid given was similar in all groups.

Figure 2 shows the mean extent of sensory block (as measured by loss of touch sensation) as a function of time. From one to three hours the adrenaline groups had a mean

Table 2. Changes in cardiovascular parameters expressed in terms of percentage of preblock values. Preblock values = 100%. Mean (SEM).

	S/B	S/BA	A/B
Highest pulse rate; %	115 (3.4)	124 (4.5)	128 (5.4)
Time spent with pulse rate > 110%; minutes	26.6 (10.7)	43.1 (15.6)	58.1 (15.0)
Time spent with pulse rate > 115%; minutes	16.6 (7.6)	30.9 (13.0)	38.4 (10.2)
Lowest systolic BP; %	82.7 (3.4)	75.6 (5.52)	77.1 (4.5)
Time spent with systolic BP < 90%; minutes	44.3 (17.4)	59.5 (16.4)	47.7 (15.4)
Time spent with systolic BP < 75%; minutes	3.1 (1.9)	28.1 (13.9)	11.9 (8.0)

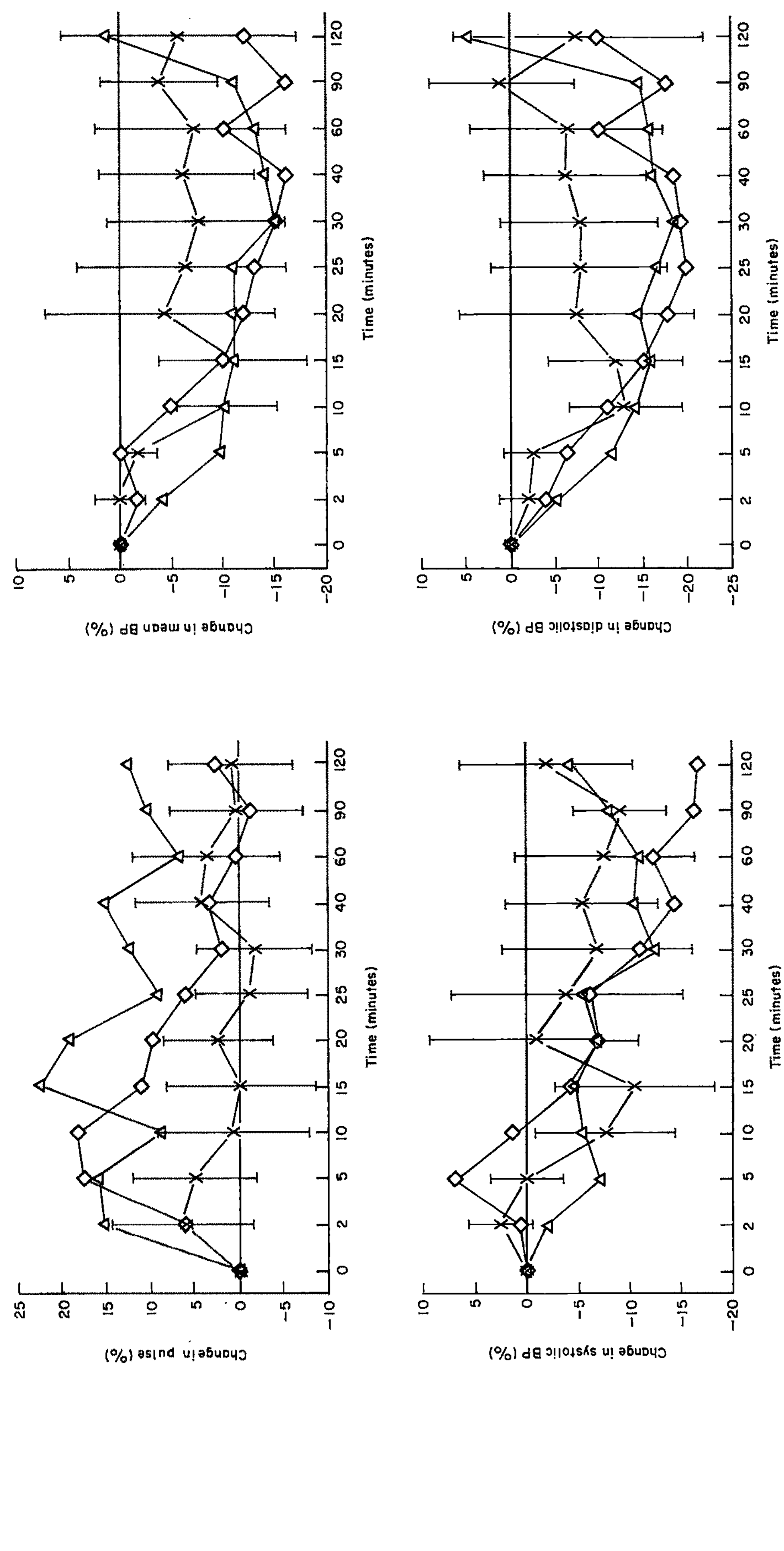

Fig. 1. Changes in mean cardiovascular parameters in the three patient groups. For the S/B group data are presented as mean (SEM 1.96) △, A/B; ◇, S/BA; ×, S/B.

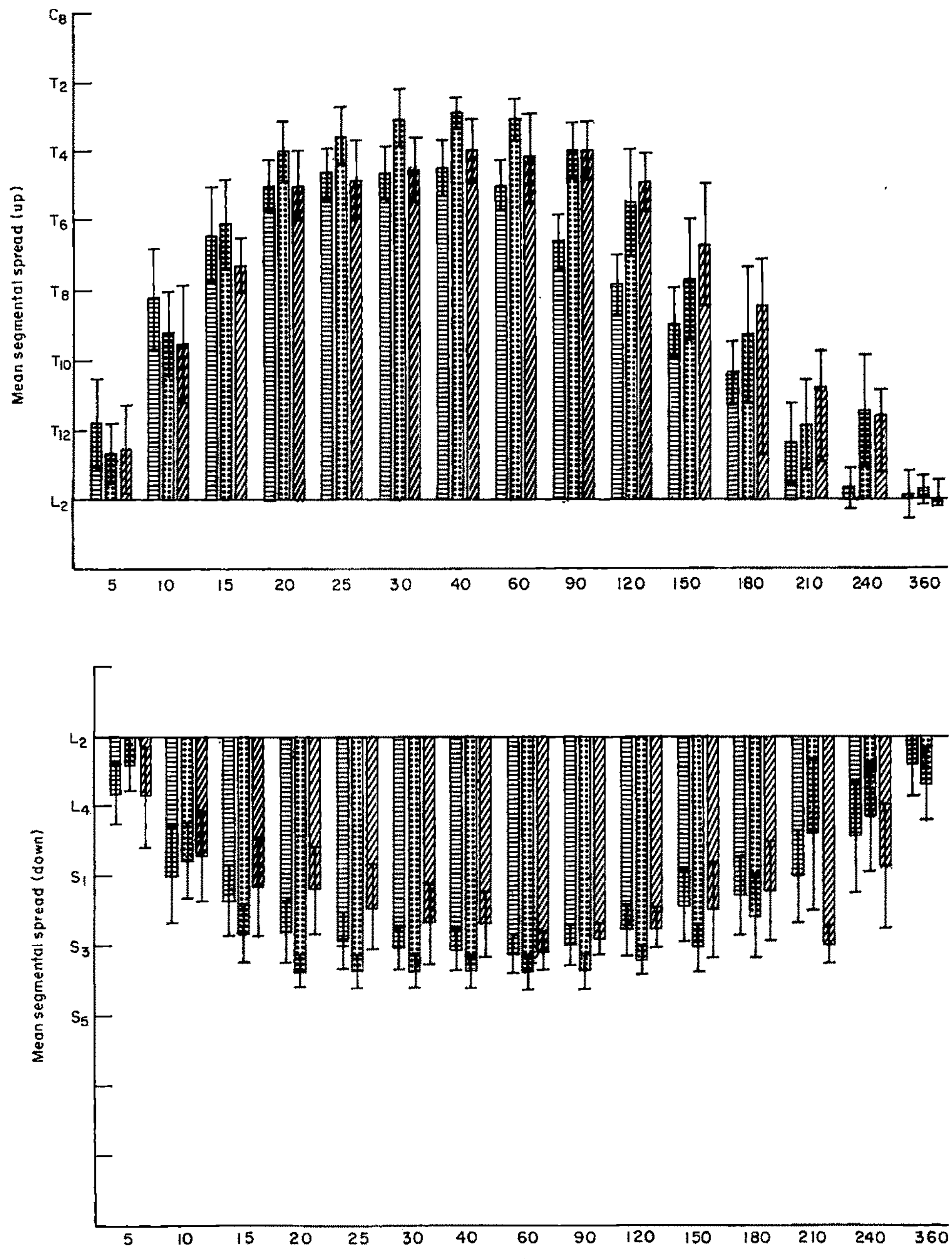

Fig. 2. Mean segmental spread of analgesia as determined by loss of sensation to a 27 G short dental needle. The top chart shows the spread in the upward direction away from the site of the catheter and the lower chart the downward spread. The data are expressed as mean (SEM 1.96) ▤, S/B; ▩, S/BA; ▨, A/B.

Table 3. Number of patients achieving analgesia to specific levels.

Level	S/B	S/BA	A/B
S_3	5	8	4
S_1	7	8	6
L_4	7	8	7
T_{12}	8	8	7
L_2–T_8	7	8	7
T_4	4	8	6
T_2	1	4	2

Table 4. Sensory block characteristics.

	S/B	S/BA	A/B
Time taken to achieve highest sensory level; minutes, mean (SEM)	22.5 (2.3)	28.1 (2.9)	32.2 (8.8)
Time spent at highest sensory level; minutes, mean (SEM)	35.9 (10.1)	31.9 (9.7)	36.3 (8.6)
Overall duration of sensory block; minutes, mean (SEM)	300 (34.8)	309.4 (36.8)	270 (42.1)

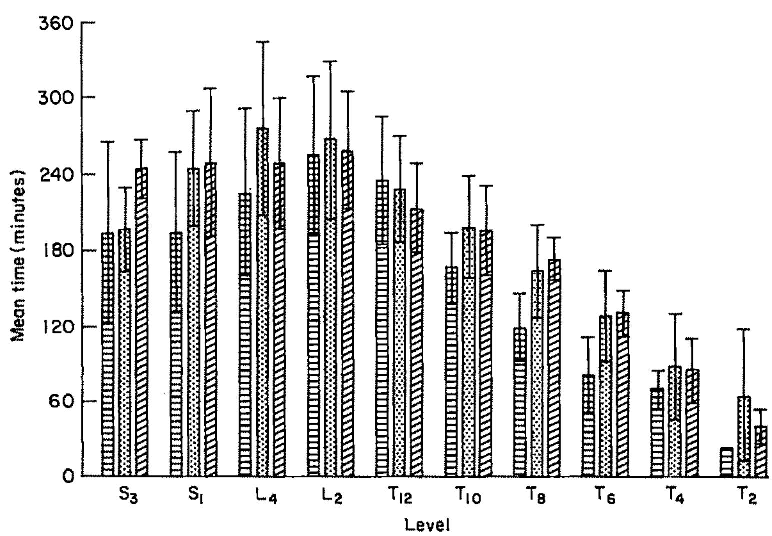

Fig. 3. Mean time (minute) at sensory block levels (SEM 1.96). ▤, S/B; ▨, S/BA; ▩, A/B.

upward spread greater than the 95% confidence limit for the S/B group.

Table 3 shows the number of patients in each group who achieved a particular height of block. The number of patients achieving a clinically useful block of T_4 or T_6 was not significantly different between the groups when the Yates' correction to the Chi-squared test was applied. Figure 3 shows the mean time spent at each block height. The time spent at T_4 (for those patients who achieved this level) was also not significantly different between the groups. However, for T_6 block the A/B group spent more time blocked at that level than the S/B group (*t*-test, $p = 0.023$) but not the S/BA group. The mean time to achieve the highest sensory block, the mean length of time spent at that level and the overall duration of sensory block are shown in Table 4 for all three groups. No significant differences were noted between the groups for these parameters.

Data on motor blockade are summarised in Table 5. The number of lower limbs in each group blocked to a grade 2 or higher was increased when adrenaline was used, significantly so in group A/B (Chi-square (Y) = 6.282, $p = 0.043$). The number of lower limbs blocked to grade 3 in the S/BA and A/B groups just failed to reach significance (Chi-square (Y) = 5.58, $p = 0.06$). The onset times for the three levels of motor blockade were not significantly different amongst the groups. However, the A/B group had a longer duration of motor block at level 1 compared to the S/B group (*t*-test, $p = 0.016$). The S/BA group also had a greater level 1 motor block duration but this just failed to reach significance (*t*-test, $p = 0.051$).

Mean plasma bupivacaine concentrations in the three groups are shown in Figure 4. Mean values of the maximum concentration (C_{max}), the time taken to achieve maximum concentration (T_{max}) and the area under the concentration/time curve (AUC) are given in Table 6.

There were no statistical differences between the maximum bupivacaine levels found, or the time to these maximum levels, although the mean level with the S/B group is higher and the time taken to reach the maximum level for the A/B group is longer. There was no statistical difference between the groups with regard to area under the curve.

Discussion

The addition of adrenaline to local anaesthetic solutions for epidural analgesia has been common practice for many

Table 5. Motor block (MB) characteristics.

	S/B	S/BA	A/B
Number of lower limbs achieving			
MB level 1	15	12	16
MB level 2	3	7	11
MB level 3	0	6	6
in minutes, mean (SEM)			
Onset time for			
MB level 1	17.8 (2.5)	15.8 (1.9)	18.8 (2.3)
MB level 2	25.0 (5.0)	52.9 (34)	39.0 (8.2)
MB level 3	N/A	75.8 (52)	56.7 (32)
in minutes, mean (SEM)			
Duration of			
MB level 1	81 (17.7)	148 (26.9)	205 (46)
MB level 2	70 (0.0)	92 (23.5)	113 (36.7)
MB level 3	N/A	74 (23.3)	100 (20.4)
in minutes, mean (SEM)			

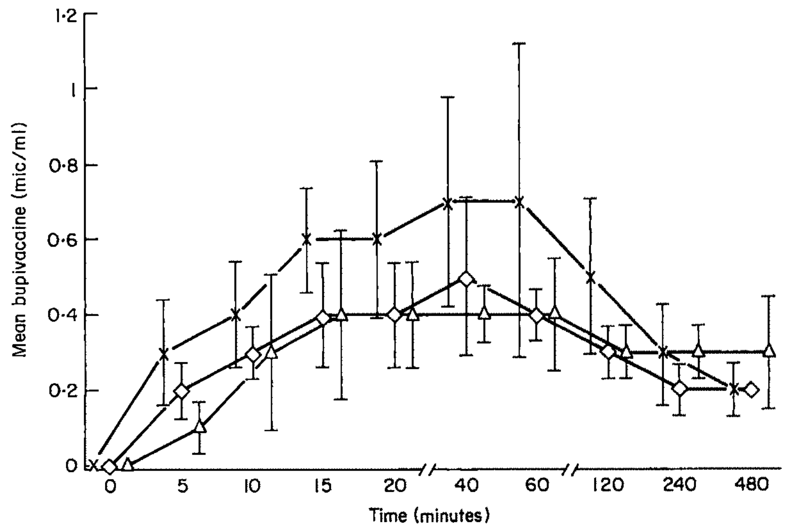

Fig. 4. Mean plasma bupivacaine concentrations (SEM 1.96). △, A/B; ◇, S/BA; ×, S/B.

years and is widely recommended in standard texts.[1,8] It has been shown that adrenaline–bupivacaine mixtures tend to produce a denser and more reliable block than when a plain solution is used.[9–11]

The addition of adrenaline lowers the peak plasma concentration of local anaesthetic but does not necessarily alter the time to attain that peak.[12] This may reflect a slow onset of action; adrenaline-induced vasoconstriction is not attained until a proportion of the dose of bupivacaine has been absorbed.[2,3]

The extent and intensity of the block, both motor and sensory, will depend upon the amount of local anaesthetic available to penetrate the neural tissue. If less local anaesthetic is eliminated as a result of a decreased blood flow in the epidural space, more drug should be available to enter neural tissues with an improved degree of blockade.[13] Thus the effect of adrenaline may not be optimal when given simultaneously with bupivacaine. We postulated that by administering the adrenaline 5 minutes before the local anaesthetic, vasoconstriction might be maximal at a time when the bupivacaine was injected. This would be expected to enhance the blockade, providing better quality sensory analgesia with lower plasma bupivacaine concentrations.

The results of this study, however, demonstrate that whilst priming of the epidural space with adrenaline tends to improve both the extent and duration of sensory analgesia, priming has no clear advantage over injecting adrenaline and bupivacaine simultaneously. Priming with adrenaline improves motor block by reducing onset time and increasing duration of block, but it is again questionable whether these minimal differences are likely to confer significant benefit in the clinical situation. Bupivacaine concentrations are seen to be reduced in the adrenaline groups; this is in agreement with the work of others.[12,14] The plasma bupivacaine levels in the two adrenaline groups do not differ significantly from each other. Pretreatment with adrenaline delays the peak absorption when compared to the bupivacaine combined with adrenaline group.

The power of this study could have been increased by use of larger patient groups. However, eight patients in each group would have given us a 90% power at the 0.05% significance for a 25% difference in maximum plasma bupivacaine concentrations.

There is some indication that adrenaline 1:200 000 may be beneficial in epidural anaesthesia. However, it seems that priming the epidural space with adrenaline confers little advantage in the clinical situation when compared to injections of bupivacaine mixed with adrenaline.

Table 6. Parameters describing the plasma bupivacaine time course.

	S/B	S/BA	A/B
C_{max}; μg/ml, mean (SD)	0.69 (0.11)	0.49 (0.11)	0.49 (0.10)
T_{max}; minutes, median value	20	20	20
AUC; μg/ml/minute, mean (SD)	190 (100)	120 (19.5)	149 (40.8)

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Anaesthesia, 1991, Volume 46, pages 1030–1032

CASE REPORT

Septic atrial thrombus

A complication of central venous catheterisation

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Summary

A 77-year-old man underwent repair of a vesicocolic fistula following which he had a protracted stay in the intensive care unit due to recurrent septicaemia, which was initially caused by bowel anastomosis breakdown. Management included central venous cannulation and pulmonary artery catheter monitoring. A septic, mobile right atrial thrombus developed, which was successfully treated. The literature on this condition is reviewed.

Key words

Heart; right atrial thrombus.
Veins; cannulation, complications.
Infection; septicaemia.

Right atrial thrombus is a recognised complication of central venous catheterisation and the incidence in patients with central catheters *in situ* has been reported to be 5%.[1] It occurs more commonly following the use of pulmonary artery catheters and polyurethane central venous cannulae. Diagnosis is made by echocardiography *in vivo*. Treatment consists of thrombolysis, anticoagulation or surgery depending on the type of clot and the condition of the patient. Mortality from clinically apparent clots is high (29%).[2]

Case history

A 77-year-old man weighing 90 kg presented for routine repair of a vesicocolic fistula. He had a past medical history of hypertension, diabetes, chronic renal failure and gout, for which conditions he was receiving frusemide, enalapril, glibenclamide and allopurinol. An anaesthetic 5 years previously had been uneventful. The surgical procedure entailed sigmoid colectomy with repair of the vesicocolic fistula. The 5 hour procedure under general anaesthesia was uneventful, with a blood loss of 500 ml. Postoperatively he was hypothermic (34°C) and in view of his chronic medical problems was admitted to the intensive care unit (ITU) for immediate management.

On the second day after admission to the ITU the patient became septic. He was pyrexial, hypotensive and oliguric. Management included the use of a pulmonary artery catheter to monitor his haemodynamic status. Continuous central venous cannulation was also required for monitoring and administration of parenteral nutrition. At this stage, bowel anastomosis breakdown was considered as a cause of his sepsis, but there was no conclusive evidence to justify a laparotomy. Investigations were undertaken therefore, to exclude other sources of infection. These included blood cultures, urine analysis, sputum, abdominal ultrasound and echocardiography, all of which proved to be negative. On day 3 haemodiafiltration was started for treatment of renal failure and was required for a further 20 days.

The patient's progress was slow due to recurrent episodes of sepsis, which resolved rapidly. Concurrent complications included atrial fibrillation and jaundice as a result of aseptic cholestasis. A tracheostomy was performed on the 27th day. On the 40th day, the patient developed signs of intestinal obstruction and again became septic. Computerised tomography (CT) showed small bowel matted together at the site of the anastomosis and suggested a paracolic abscess. A barium enema confirmed suspicions of an anastomotic leak, for which a defunctioning colostomy was performed.

The patient gradually improved, but continued to have a low-grade pyrexia, for which numerous investigations were undertaken. These included a negative lumbar puncture and abdominal ultrasound. However, on the 60th, 67th and 74th days he developed recurrent episodes of septicaemia. A repeat CT scan was performed on the 69th day, which showed that problems associated with the operative site were resolving, and no focus of infection was seen. On the 78th day, a white cell radioactive tracer scan (Fig. 1) was

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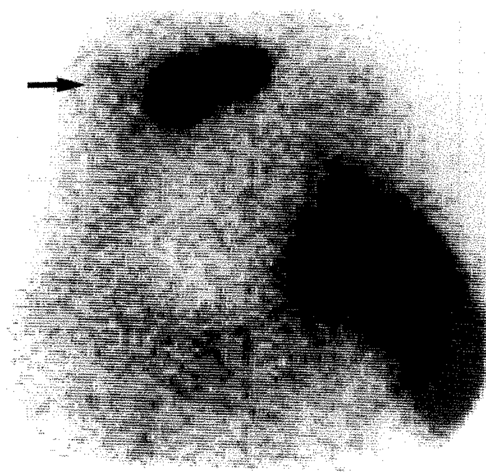

Fig. 1. White cell radioactive tracer scan of thorax. Arrow denotes hot spot corresponding to septic atrial thrombus.

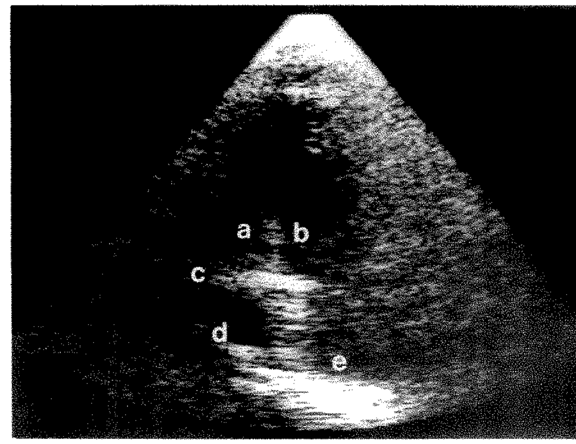

Fig. 2. Echocardiogram showing presence of septic atrial thrombus (c). Right atrium (a), left atrium (b), right ventricle (d), and left ventricle (e) are clearly visible.

performed, which displayed a hot spot anteriorly in the upper mediastinum. Consequently a repeat echocardiogram (Fig. 2) was performed which exhibited a bright area of echogenicity in the right atrium adherent to the anterior leaflet of the tricuspid valve; no evidence of endocarditis was observed. The diagnosis of a septic thrombus of the right atrium was made.

Management of the septic thrombus included heparin anticoagulation together with teicoplanin and gentamicin. However, the antibiotic regimen was later changed to imipenem, teicoplanin and metronidazole, after *Staphylococcus epidermidis* and *Pseudomonas aeruginosa* had been cultured. A further echocardiograph performed 5 days later showed a resolving area of echogenicity. This had completely disappeared at follow-up at 14 days. The patient's condition simultaneously improved, with the resolution of the pyrexia, a return to enteral feeding and complete independence from the ventilator. The patient was eventually transferred back to the general surgical ward on day 90.

Discussion

Right atrial thrombus is a well known complication of central venous cannulation. It is difficult to estimate the true incidence from the available literature. A 1-year prospective study of 141 postmortems in patients with a central catheter present at the time of death by Ducatman *et al.*[1] showed a 32% incidence of all thrombi in the right side of the heart. Atrial thrombi occurred in 5% of the patients. In this study, pulmonary artery catheters had a higher incidence (33%) of thrombosis than right atrial catheters (29%). However, this may not reflect the true incidence *in vivo*. Other predisposing factors include hyperalimentation[3,4] and the nature of the catheter material.[5] Polyurethane and silicone catheters are the most thrombogenic, whereas polyurethane catheters coated with hydromer are the least.

The incidence of septic atrial thrombus is unknown. It may be associated with infections complicating central venous cannulation,[6] the incidence of which has been reported as 7–16%[7] and may be greater during parenteral nutrition. However, Ducatman *et al.*[1] concluded that the presence of a right heart thrombus may not be associated with an increased incidence of septicaemia.

Right atrial thrombus can present with paroxysmal syncope, chest pain, dyspnoea or arrhythmias. It can cause morbidity or mortality by obstructing blood flow as a result of a ball valve action, by embolising to the lungs, or by becoming a source of infection.[2]

A review of all atrial thrombi reported between 1981 and 1988 by Crowell *et al.*[2] discussed the diagnosis, classification and treatment. Diagnosis is best achieved by comprehensive echocardiography, which should include real-time, two-dimensional parasternal and apical views. As a result, atrial thrombi may be classified as mobile or fixed, and the type of thrombus influences the approach to treatment. The three available options are anticoagulation, thrombolysis and surgery. Anticoagulant therapy in patients with a mobile atrial thrombus appears to be associated with a higher risk of sudden dissolution and subsequent fatal pulmonary embolus. Surgery should be considered in this group if the patient's condition is stable. Fixed atrial thrombi respond well to fibrinolytic therapy and are associated with a lower incidence of embolism. Mobile clots produce a higher overall mortality (33%) than fixed clots (20%).[2] In this review, the combined mortality of both groups of atrial thrombi diagnosed *in vivo* was 29%. However, in the study by Ducatman *et al.*, although the frequency of atrial thrombosis at postmortem was 5%, no mortality was attributed to the thrombosis. It would appear that atrial thrombus diagnosed *in vivo* has a greater mortality.

The patient we reported responded well to anticoagulant and antibiotic therapy, with resolution of the clot and the septic episodes. Pulmonary artery catheterisation, parenteral nutrition and prolonged central venous cannulation may all have played a part in the development of the lesion. This case reinforces the recommendation by Smith and Kaye,[7] that any patient who has had central venous cannulation and develops an unexplained septicaemia, should undergo echocardiography.

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CASE REPORT

Serious complications with dextran-70 despite hapten prophylaxis

Is it best avoided prior to delivery?

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Summary

Dextran is used clinically for plasma volume expansion, improvement of blood flow and thromboprophylaxis, but has been associated with untoward side effects. Immunoprophylaxis with dextran I (hapten), before the infusion of dextran-70, has reduced the incidence of serious dextran-induced anaphylactoid reactions. We report three cases of severe reactions occurring during anaesthesia in spite of immunoprophylaxis. One patient given dextran-70 before Caesarean section had a mild reaction but gave birth to a child with serious brain damage. One patient with an extremely high titre of dextran-reactive antibodies died from myocardial infarction and another patient recovered without sequelae. From our experience we conclude that dextran-induced anaphylactoid reactions are still a serious problem despite immunoprophylaxis. Dextran-70 should be avoided during pregnancy and should not be given during Caesarean section before delivery of the child. Even in the presence of immunological prophylaxis, vigilant observation of the patient is essential and resuscitation equipment must be available when starting a dextran infusion.

Key words

Immunophrophylaxis; dextran 1.
Complication; anaphylaxis.

The efficacy of dextran-70 as a volume expander and in thromboprophylaxis has led to its extensive use during surgery. In Scandinavia the compulsory registration of side effects of drugs has showed several serious complications associated with its use. In Sweden, 28 deaths were reported between 1970 and 1979 and it became evident that some patients had dextran-reactive antibodies (DRA) in high titres[1] making them susceptible to severe dextran-induced anaphylactoid reactions (DIAR). The pathophysiological mechanism of DIAR in man is an immune complex-mediated anaphylaxis.[2] Multicentre studies showed that immunological prophylaxis with dextran 1 (hapten) could reduce the incidence of DIAR dramatically.[3]

In our hospital about 15 000 patients are anaesthetised each year. We use dextran-70 as our routine thromboprophylactic both per- and postoperatively, and the drug is given to about 3000 patients per year. Before the start of an infusion of dextran we routinely administer 20 ml of 15% dextran 1 (Promiten). We report three patients who, in spite of hapten prophylaxis, developed a severe reaction to dextran-70.

Case histories

Patient 1

A 34-year old pregnant woman, previously healthy except for a history of allergic skin reaction to penicillin, was admitted to hospital for an elective Caesarean section for cephalopelvic disproportion. The pregnancy was uncomplicated, except for a tendency to syncope when in the recumbent position.

An epidural block was performed at the L_{2-3} interspace, and the catheter was introduced 5 cm into the epidural space. The patient was given 500 ml of Ringer's solution, and an epidural test dose of bupivacaine 0.5% 3 ml was given without any untoward reaction. The patient was placed in the supine position, with a 15° left lateral tilt.

Chloroprocaine 3% 15 ml was injected epidurally, and a further intravenous infusion of 1000 ml of Ringer's solution was given. Dextran 1 20 ml was given intravenously, and 3 minutes later an infusion of dextran-70 was started. When 50 ml had been infused, the patient started to feel uneasy, developed nausea, a skin rash, and peri-orbital

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oedema. She developed bronchospasm and the systolic blood pressure fell to 75 mmHg. Dextran-70 was immediately stopped and the crystalloid infusion was accelerated. She was given ephedrine in repeated doses, calcium chloride and hydrocortisone. She remained conscious and breathing oxygen by mask.

The circulation was stabilised in a few minutes, and the systolic blood pressure was never less than 75 mmHg. The fetal heart sounds were not monitored during the reaction.

After 20 minutes the patient had fully recovered and the Caesarean section was performed under epidural anaesthesia with a sensory block extending to T_6. At delivery the baby's heart rate was 20 beats a minute. The obstetrician observed an oedematous umbilical cord. The baby was successfully resuscitated, but later demonstrated signs of severe brain damage and died from pneumonia at 18 months old. The mother's dextran-reacting antibody titre was 1024 before infusion of dextran-70, and 512 later the same day.

Patient 2

A previously healthy 53-year old man was admitted to hospital for urolithiasis surgery. After arrival in the operating theatre a crystalloid infusion was established and 20 ml 15% dextran 1 was given. Three minutes later a dextran-70 infusion was started. When 150 ml had been infused the patient experienced itching and a skin rash was observed. The dextran infusion was stopped and he was given intramuscular and intravenous adrenaline 0.5 mg and 0.2 mg respectively, intravenous promethazine chloride 12.5 mg, and the crystalloid infusion was accelerated. In spite of immediate treatment the blood pressure fell and increasing exanthema was observed. The patient was breathing oxygen by mask and ventilation was intermittently assisted. The condition gradually worsened and transiently the blood pressure could not be measured. Twenty-five minutes after the onset of symptoms his condition gradually improved.

A total of 6 litres of Ringer's solution, adrenaline 0.9 mg, metaraminol 0.8 mg, and hydrocortisone 300 mg was given. Arterial blood gases showed adequate oxygenation and normal acid/base status. However, the patient had an unstable circulation and needed a dopamine infusion for about 24 hours after the reaction. The patient recovered without sequelae and the operation was performed uneventfully 3 days later. The dextran-reactive antibody titre pre-operatively was found to be 1024 and 512 on the fourth day after the event.

Patient 3

A previously healthy 64-year-old man was admitted for elective hernia surgery. Pre-operative electrocardiograph and standard blood tests were normal. A spinal block was performed at L_{3-4} with 1.8 ml lignocaine 5% in glucose, which produced a sensory block to the level of T_{10}. Infusion of Ringer's solution was started and 20 ml 15% dextran 1 was administered. Five minutes later an infusion of dextran-70 was started. After infusion of 100 ml, and 20 minutes after the commencement of the spinal blockade, the patient became nauseated. The systolic blood pressure was 80 mmHg. He was given ephedrine 10 mg, atropine 0.5 mg and intravenous metoclopramide 10 mg. He was breathing oxygen by mask. No bronchospasm or skin reactions were observed. The patient's condition continued to deteriorate despite further treatment with adrenaline and atropine. Eventually he developed arrhythmias and circulatory arrest. Immediate resuscitation was started and his trachea was intubated and lungs ventilated with 100% oxygen. Adrenaline was given in repeated doses and after 45 minutes he regained spontaneous circulation with a systolic blood pressure of 50 mmHg. Despite active treatment the patient died 2 days later of brainstem herniation.

The dextran-reactive antibody titre was found to be 524 288 pre-operatively and 2048 10 hours after dextran infusion. Autopsy showed severe cerebral oedema and a small myocardial infarction.

Discussion

Serious complications still occur in spite of immunoprophylaxis when dextran-70 is administered. The dextran-induced anaphylactoid reaction occurs when polyvalent high molecular dextran (e.g. dextran-70) forms large immunocomplexes with circulating dextran-reactive antibodies (DRA). The immunocomplexes initiate activation of platelets, leucocytes, the complement system, and the coagulation system with concomitant vasoactive mediator release leading to the symptoms of anaphylaxis.[5] The titre of DRA is related to the degree of anaphylactic reaction. The titres in our patients were determined by passive haemagglutination of stearoyldextran-coated human erythrocytes with serial twofold dilution of test serum. The tests were performed by the laboratory of Pharmacia AB, Sweden.

Low molecular dextran (dextran 1) acts as a hapten, and blocks the antigen combining sites of the preformed DRA without causing any immunological reaction. The hapten-DRA binding prevents the formation of large DRA–dextran-70 immunocomplexes which trigger DIAR.

Ljungstrøm *et al.*[6] found a reduction from 22 severe DIAR per 100 000 administrated units of dextran-70 without hapten prophylaxis, to 1.2 severe DIAR per 100 000 administrations with hapten prophylaxis.

Dextran-reactive antibodies (DRA) exist in low titre in most human beings, and the patients developing the most serious dextran-induced anaphylactoid reaction (DIAR) usually have high DRA titres.[2] The DRA are formed in response to high molecular weight polysaccharides either as dextranes or bacterial polysaccharides. Dextranes ingested as contaminants of sucrose or as components of dental plaques or produced by the microflora in the gastrointestinal tract, may induce antibody formation. Cross-reaction between antibodies against bacterial wall polysaccharides and clinical dextran is another possibility for the formation of DRA.[4]

Patient 1 is of particular clinical interest. Reviews of this case by the hospital's legal board and also by the company producing dextran-70 (Pharmacia AB, Sweden), conclude that a DIAR is the likely cause of damage to the child. The haemodynamic changes in the mother, however, do not provide the full explanation of the tragic outcome for the child. The umbilical cord was oedematous, and this may reflect an anaphylactoid reaction in the child but no information is available about whether DRA or hapten crosses the placenta barrier. Another possible mechanism is

asphyxia caused by placental circulatory insufficiency as a result of microembolism of immunocomplex-aggregates. Vascular microembolism in the lungs is a common finding in autopsy studies after fatal DIAR[5] but in our case the placenta was not studied histologically.

Patient 2 demonstrates a serious DIAR, with adequate handling and uneventful recovery. It is, however, of interest to note the difference in reaction pattern between patient 1 and patient 2 though both had the same pre-operative DRA titre. This difference in reactivity may be explained from nonantibody mechanisms and also from different DRA subclass composition[7] and binding with dextran 1.

Patient 3 had extremely high titres of DRA. The dose of 20 ml dextran-1 15% is calculated to be sufficient for neutralisation of high titres of DRA but will not be sufficient for the extreme titres that occurred in our patient.[7] This patient further demonstrates the occasional difficulty of diagnosing DIAR during anaesthesia.

The rare but severe complications to the use of dextran-70 forces the clinician to take several precautions when deciding to use this drug. Firstly, pregnancy should be regarded as a contraindication against its use. The drug may cause complications to the child that are difficult to monitor and treat. Specifically, after experiencing case 1 we do not use dextran-70 during Caesarean section before delivery is completed. Secondly, the need for the immediate availability of resuscitation equipment and drugs must be stressed. In circulatory collapse adrenaline should be the drug of first choice. Thirdly, the start of every administration should be slow to allow for observation of anaphylactoid reactions.

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CASE REPORT

Reversal of prolonged suxamethonium apnoea with fresh frozen plasma in a 6-week-old infant

R. S. GILL, N. O'CONNELL AND R. P. F. SCOTT

Summary

A period of apnoea lasting 480 minutes following suxamethonium in a 6-week-old male infant is described. Neuromuscular function recovered following the administration of fresh frozen plasma. The infant was found to be homozygous for atypical cholinesterase ($E_1^a E_1^a$). This is believed to be the youngest reported case of suxamethonium apnoea.

Key words

Neuromuscular relaxants; suxamethonium.
Complication; prolonged apnoea.
Enzyme; plasma cholinesterase.

Case history

A 6-week-old, 5 kg, Caucasian male infant presented for correction of bilateral club feet. He was born by spontaneous vaginal delivery after a normal pregnancy and had been in good health since birth. Neither his parents nor his three siblings had previously received anaesthesia.

No premedication was prescribed. Anaesthesia was introduced by a gaseous induction, with oxygen, nitrous oxide and halothane using a Mapleson F system. A 22-G catheter was inserted into a vein in the dorsum of his left hand. Intravenous atropine 0.1 mg was administered followed by 8 mg suxamethonium, and the patient's trachea was intubated with a 3 mm Portex orotracheal tube. Anaesthesia was maintained with oxygen, nitrous oxide, enflurane and 1.5 mg of intramuscular papaveretum. Ventilation was controlled manually intra-operatively; the electrocardiogram, blood pressure, oxygen saturation and end-tidal carbon dioxide were monitored continuously and maintained within normal limits. The procedure lasted for 2.25 hours and at completion, the child remained apnoeic despite being normothermic and normocapnoeic. It was considered enough time had been allowed to eliminate any volatile agent and therefore naloxone 80 μg was administered to reverse any opioid-induced central depression, but without effect. A Duostim peripheral nerve stimulator was used to test for residual neuromuscular blockade, using fine subcutaneous needle electrodes at the wrist to stimulate the ulnar nerve. No response to train-of-four or tetanic stimulation could be detected by tactile evaluation of the force of contraction of the adductor pollicis muscle. A provisional diagnosis of suxamethonium apnoea was made. A blood sample was taken for emergency cholinesterase activity, electrolytes and blood gas analysis. The child was transferred to a postoperative high dependency unit where intermittent positive pressure ventilation was instituted with nitrous oxide and oxygen.

Serum electrolytes and arterial blood gas analysis were within normal limits. A cholinesterase activity level of 1116 international units per litre (IU/litre) was reported as possibly low, but no reference range was available for a child of this age; the normal adult range is 3700–11 500 IU/litre. Seven and a half hours following the end of surgery, there was still no response to train-of-four nerve stimulation. Fade in the force of contraction of the adductor pollicis was, however, detectable following tetanic stimulation of the ulnar nerve at 50 Hz for 5 seconds. It was decided to give the child 40 ml of fresh frozen plasma over 0.5 hour in addition to his maintenance fluids. Neuromuscular function, as assessed by the response of the adductor pollicis to train-of-four stimulation of the ulnar nerve, returned to normal after 15 minutes. The child was extubated awake and active. He remained in the high care unit for a further 4 hours with no problems before returning to the ward.

Serum was taken from the child and his family for cholinesterase assay, dibucaine and fluoride number estimation. The patient was found to be homozygous ($E_1^a E_1^a$) for atypical cholinesterase with low dibucaine and fluoride numbers. His family are described in Figure 1.

The family and their general practitioner were informed

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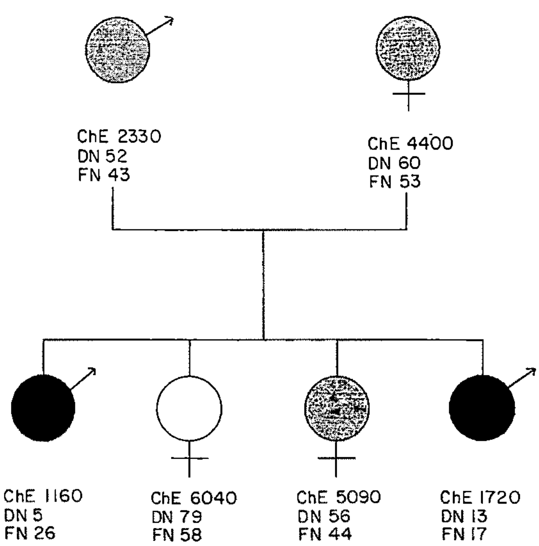

Fig. 1. The family's genotyping and plasma cholinesterase. Normal values: plasma cholinesterase, 3700–11500 IU/litre;[1] dubicaine, 77–83;[2] fluoride number 57–65.[2] ○, $E_1^uE_1^u$; ●, $E_1^aE_1^a$; ◍, $E_1^u E_1^a$.

of the results and the two male children have been issued with warning cards.

Plasma cholinesterase activity was measured by the method of Knedel and Bottger[1] at 25°C using a Perkin Elmer 550S spectrophotometer with the Boehringer Mannheim GmbH 'cholinesterase C-system' commercial kit. This uses cholinesterase catalysed hydrolysis of butyrylthiocholine to thiocholine, which is coupled to the further reaction of thiocholine with dithiobis, measuring the absorbance change at 405 nm.

Inhibitor numbers were measured at 25°C as described by Varley.[2] Cholinesterase activity is measured by means of its catalysis of hydrolysis of benzoylcholine (200 nmol). The change in absorbance at 240 nm is monitored as a function of time, with and without the addition of dibucaine and fluoride inhibitors. The inhibitor numbers are then calculated from the equation:

$$\%\text{ inhibition no} = \left(1 - \frac{\Delta A \text{ with inhibitor}}{\Delta A \text{ without inhibitor}}\right) \times 100$$

Discussion

Plasma cholinesterase (ChE) is synthesised in the liver.[5] To date, no unequivocal role has been assigned to ChE but it may play a part in the transmission of slow nerve conduction processes[6] or lipid metabolism[7] or a regulatory role in conjunction with choline acetylase in choline homeostasis in plasma.[18]

The normal serum ChE level is 3700–11500 IU/litre. Abnormally low serum ChE levels occur in liver failure,[9] anaemia,[10] ureamia,[11] pregnancy and postpartum,[12] after therapeutic irradiation,[13] after contamination with organophosphorous compounds[14] and as familial abnormality in about 1 in 3000 of the population.[15]

Reports conflict with regard to the influence of age and sex on the level of ChE activity in both children and adults. The ethnic origin of the individuals in all the surveys has been Caucasian. At birth, the activity of ChE is approximately 50% of nonpregnant adults.[16] There is disagreement about ChE activity in the first 6 months of infancy. According to earlier reports, there is a dramatic increase in the activity during the first 3 weeks of life to a value greater than that of the healthy adult, and which persists until the third year.[17] More recently, it has been suggested that activity remains at about 50% of the adult value until 6 months. The mean ChE activity of 1024 children of between 3 and 6 years, was found to be 30% above the adult level,[18] decreasing from the age of 5 years to reach adult levels by puberty.[19]

In this case, the homozygous infant aged 6 weeks had an activity approximately 40% that of the lower end of the normal adult range. Interestingly, the 480 minute period of apnoea was substantially longer than that usually seen in the atypical homozygote.[20] The Danish Cholinesterase Research Unit reported an average apnoea time of 92 minutes from 105 homozygous patients (range 25–40 minutes). As might be expected, their study showed the longest apnoeic time in patients homozygous for the silent gene (average 170 minutes, range 70–330 minutes). This again emphasises the difference in infants as the average age of their patients was 38 years.

Stored blood and its products have been used in the treatment of prolonged suxamethonium apnoea. One thousand ml of bank blood has been successfully used to reverse a prolonged apnoea in an atypical homozygous adult.[21] Plasma cholinesterase activity has been shown to fall to 87% of activity when measured in blood banked in various mediums, after storage for 21 days at 4°C.[22–24] Eighty per cent of the small decrease in activity occurs during the first 2 days of storage; the cause of this is uncertain but it has been related to the presence of red cells.[25] Freshly separated plasma shows no decline in activity of ChE for 5 days stored at 0°C, and no decline in activity when stored for 7 weeks at −70°C. A purified form of human cholinesterase has been used to treat prolonged suxamethonium apnoea. An intravenous dose of 90 mg of this preparation re-established spontaneous respiration in 10 minutes.[26] Forty-five mg of the enzyme concentrate has the cholinesterase activity of 500 ml of fresh human plasma.

Although the use of blood products and the purified human enzyme have been shown to work, their use is still contentious, since supportive ventilatory therapy will eventually have the same outcome without the additional risks associated with administering blood products.

In the case reported, it was decided that since the period of apnoea was so long, and there was concern regarding the aetiology of the apnoea, a rapid response to fresh frozen plasma would provide a useful diagnostic, as well as therapeutic manoeuvre. In view of the risks associated with administration of blood products, we would not recommend this approach for any shorter period of apnoea.

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Anaesthesia, 1991, Volume 46, pages 1039–1040

CASE REPORT

Respiratory failure as presentation of achalasia of the oesophagus

A. P. KENDALL AND E. LIN

Summary

A 68-year-old woman with a history of hiatus hernia developed aspiration pneumonia after operation for fractured neck of femur. After 8 days, acute respiratory failure was caused by massive retention of air and food in the oesophagus. This was relieved by aspiration, and treated by balloon dilation of the gastic cardia.

Key words

Complications; achalasia, respiratory failure.

Case history

A 68-year-old woman was admitted with a fractured right neck of femur. Previous medical history included an uncomplicated cholecystectomy (1975); diagnosis of hiatus hernia (1982); a fracture of the left femur requiring open reduction and internal fixation (1987). During this operation, the patient regurgitated gastric contents and suffered an aspiration pneumonia, as a result of which she spent a period of time on the intensive care unit. Apart from occasional reflux of food and a preference for a soft diet the history was unremarkable, with a good exercise tolerance. Her dynamic hip screw was positioned under spinal anaesthesia (3 ml of 0.5% bupivacaine in glucose). She made a good postoperative recovery, was mobilising well and due to be sent home on the 8th postoperative day. The night before discharge, the patient was found cyanosed, acutely short of breath and complaining of a sensation of suffocation. Medical and then anaesthetic assistance was requested.

The patient was wedged upright, pink (whilst breathing 8 litres/minute of oxygen via a Hudson mask), sweating, stuporous (responding to stimulation) with dilated pupils. Her pulse was bounding at a rate of 110 bpm and her blood pressure was 270/150 mmHg. She had a swinging jugular venous pulse and a triple rhythm, a tachypnoea of 30 bpm, and inspiratory stridor. Her trachea was central, with equal but very diminished movement; her accessory muscles were in use and she had some see-saw movement. The percussion note was resonant throughout the lung fields and the breath sounds were obscured by the stridor.

Arterial blood gas analysis showed a pH 7.11, $Pa\text{O}_2$ 18.7 kPa, $Pa\text{CO}_2$ 10.6 kPa and bicarbonate 25.4 mmol/dlitre. An electrocardiogram showed an S1Q3T3, identical to one taken pre-operatively (apart from sinus tachycardia). Chest X ray was difficult to assess, but excluded pneumothorax and upper lobe divergence and there was a question of air along the right upper heart border (the preoperative film showed this to be irregular).

Her condition was deteriorating; her level of consciousness was decreasing and so direct laryngoscopy was performed to exclude the presence of a foreign body (she did not have dentures). This was normal and demonstrated that her gag reflex was strongly present. During this time the arterial blood gas analysis and chest film was repeated (Fig. 1). This showed what appeared to be an air-containing cavity extending from the mediastinum (Fig. 2). This was thought to be air in the oesophagus and an 18 gauge nasogastric tube was passed. Five hundred millilitres of 'Complan' and air was aspirated and chest movements improved immediately. The patient regained consciousness within 3 minutes and was requesting tea soon afterwards.

Arterial blood gas analysis then returned, with a pH 6.88, $Pa\text{O}_2$ 21 kPa, $Pa\text{CO}_2$ 19.8 kPa, and bicarbonate 28 mmol/dlitre. These were repeated one hour later whilst breathing air and apart from mild hypoxaemia, had returned to normal (pH 7.35, $Pa\text{O}_2$ 8.8 kPa, $Pa\text{CO}_2$ 5.8 kPa, bicarbonate 24.7 mmol/dlitre). A barium swallow 4 days

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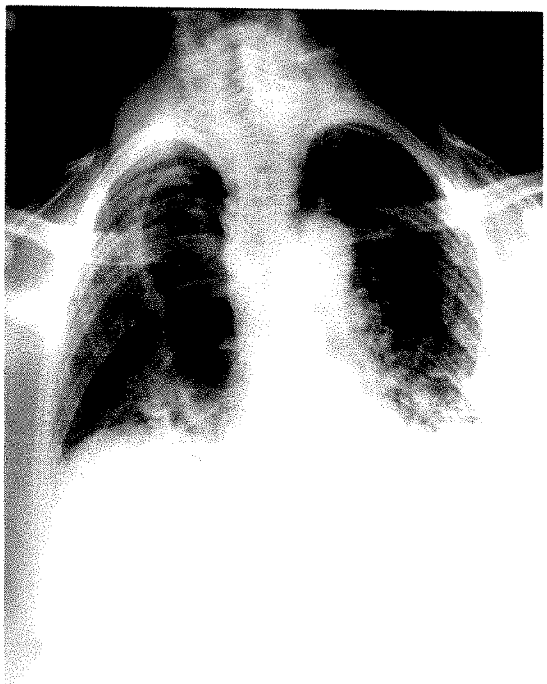

Fig. 1. Chest radiograph showing air in the dilated oesophagus.

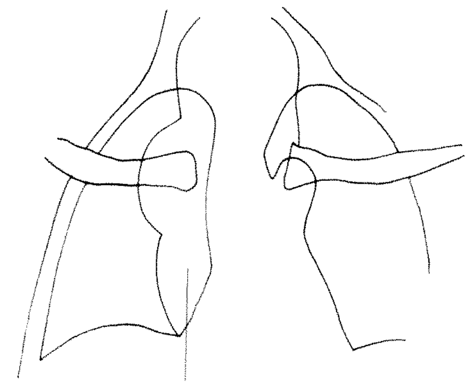

Fig. 2. Drawing showing the features of Figure 1.

later still showed food residue but endoscopy confirmed a diagnosis of achalasia of the oesophagus and the presence of two small benign gastric ulcers. The achalasia was successfully treated by balloon dilatation.

Discussion

Acute dilatation of the oesophagus causing respiratory obstruction is an uncommon presentation of achalasia. It has been described previously by Giustra *et al.*[1] with further cases by Travis[2] and Collins and Rabie.[3] McLean *et al.* described acute obstruction during recovery from anaesthesia.[4] The mechanism is unclear. The cricopharyngeal sphincter has been shown to be incompetent during inspiration[5] and may act as a one-way valve as suggested by King;[6] this would lead to the oesophagus dilating. In doing so, forward displacement of the oesophagus might occur[4] with compression or angulation of the trachea on the sternum (facilitated by its soft posterior wall). This theory has radiographic support[7] and attempts at intubation and ventilation have demonstrated the presence of subglottic obstruction.[2,3] It is probably the best explanation of the clinical situation seen in this patient.

The most successful treatment is to decompress the oesophagus with a nasogastric tube. This may not be easy to pass and cases requiring endoscopic assistance have been described. On one occasion, direct incision of the oesophagus by a collar incision was necessary to allow ventilation.[3] Other complications of this condition include aspiration pneumonia[2,3] and superior vena caval compression.[6] Chronic airway obstruction has been described where the oesophageal intrathoracic obstruction was demonstrated using a flow-volume loop.[8]

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Anaesthesia, 1991, Volume 46, pages 1041–1043

CASE REPORT

A serious complication of minitracheotomy

A. I. McEWAN, G. A. FRANCIS AND J. T. CLARKE

Summary

A previously unreported complication of minitracheotomy is described. The minitracheotomy introducer was lost into the pleural cavity and a thoracotomy was required to remove it.

Key words

Equipment; minitracheotomy.
Complications; misplaced introducer.

Minitracheotomy has become increasingly popular in recent years. However, there have been a number of case reports in the literature of complications of this technique, some of them serious. We report a new complication.

Case history

A 44-year-old woman with severe rheumatoid arthritis was referred to the regional neurosurgical centre for assessment of bulbar symptoms. A magnetic resonance imaging scan showed compression of the medulla oblongata by the odontoid peg. She therefore underwent surgery which involved removal of the odontoid peg and body of C_2 with a Luque rectangle fusion from occiput to T_1. A tracheostomy was performed under local anaesthesia prior to surgery to facilitate the transoral approach used in this procedure. Postoperatively she was allowed to breathe spontaneously and was able to maintain adequate ventilation. However, she continued to experience difficulty in swallowing, with nasal regurgitation of oral fluids and therefore the tracheostomy was left *in situ*. A decision was made on the 10th day to remove the tracheostomy tube but swallowing remained a problem and so a nasogastric tube was inserted to facilitate feeding. She was discharged back to the referring hospital on the 16th day.

She developed a chest infection 2 days after return to the referring hospital and became progressively unwell. She was transferred to the intensive care unit where a diagnosis of aspiration pneumonia was made. She received standard management with oxygen, antibiotics and physiotherapy, and a minitracheotomy was inserted with some technical difficulty. The patient suffered a respiratory arrest within hours and during the resuscitation a formal tracheostomy was required in order to secure the airway; again the procedure was noted to be difficult. A chest X ray showed a linear opacity, but the significance was not recognised. The tracheostomy tube became blocked on the following day but it was removed because she was able to maintain her own airway. Another minitracheotomy was then inserted

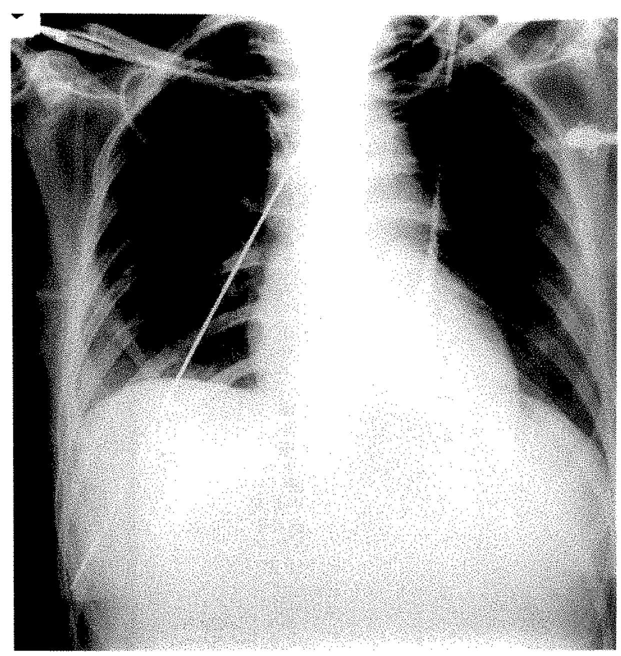

Fig. 1. Chest X ray showing minitracheotomy introducer in the right hemithorax.

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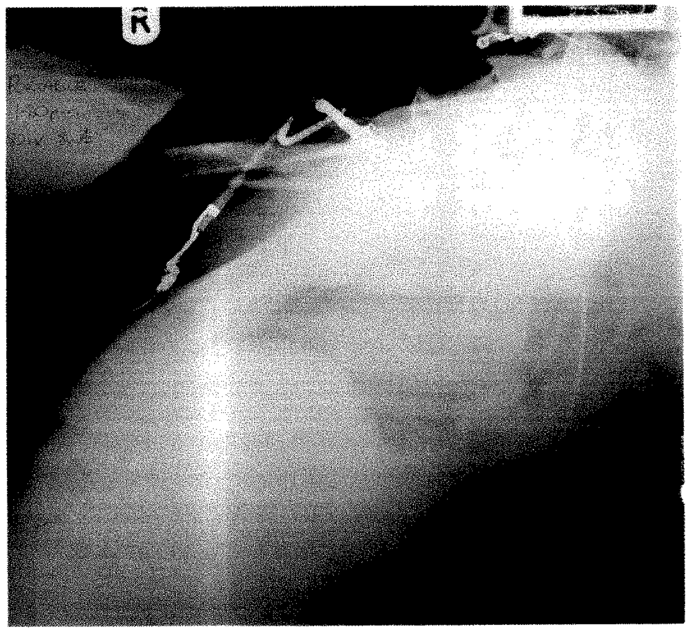

Fig. 2. Lateral chest X ray. The minitracheotomy introducer can be seen lying posteriorly.

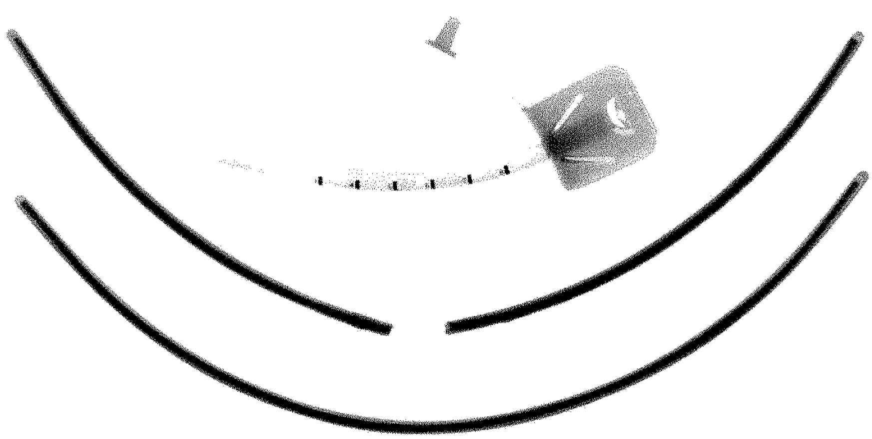

Fig. 3. Minitracheotomy tube and introducer, which was cut during the thoracotomy to facilitate its removal. An uncut introducer is shown for comparison.

to facilitate bronchial toilet. A chest X ray the next day revealed the same foreign body in the right hemithorax (Figs 1 and 2) and it was identified as a minitracheotomy introducer. She was therefore referred to the regional cardiothoracic centre for further management. Fibreoptic bronchoscopy and oesophagoscopy under light sedation failed to reveal the introducer. It was decided, in view of her poor respiratory function, to proceed to a right limited thoracotomy to avoid the risks of extensive surgery. The introducer was retrieved successfully from the right intrapleural space (Fig. 3). The patient required ventilatory support for 6 days postoperatively but by the 10th day she was considered fit enough for transfer back to the referring hospital. However, she made poor progress and died 3 months later.

Discussion

Minitracheotomy has been described as a new, simple, technique which may be used as part of the treatment for patients with sputum retention.[1,2] Other indications for its use include the treatment of respiratory failure with a high frequency jet ventilator,[3] obstructive sleep apnoea,[4] and as an emergency measure in patients with acute upper airway obstruction.[5]

The incidence of complications is unknown. Brantigen and Grow[6] reported a complication rate of 6% in a review of 655 cricothyrotomies. However, all of these cricothyrotomies were performed by thoracic surgeons who had been trained in the procedure, some surgical dissection was used, and an ordinary tracheostomy tube was inserted. Thus, the

rate of 6% quoted in this study and in a recent editorial[1] cannot be assumed to reflect the incidence of complications using a minitracheotomy.

However, there have been several case reports in the literature reporting complications of minitracheotomy. These include misplacement,[7] bleeding,[8–11] subglottic stenosis,[12] displacement during high frequency jet ventilation,[13] and inhalation of the minitracheotomy tube.[14,15] We are unaware of any other report in the literature of a minitracheotomy introducer being lost in the pleural space.

There are a number of factors which may have contributed to this potentially fatal situation. The decision to remove the original tracheostomy while the patient still had some bulbar symptoms may have been premature and possibly contributed to the development of her aspiration pneumonia. If the deterioration in her respiratory function which resulted in her admission to the intensive care unit was secondary to an aspiration pneumonia rather than simple sputum retention, tracheostomy would have been a more appropriate treatment than minitracheotomy. Inability of the patient to extend her neck would have made location of the cricothyroid membrane difficult, thus hindering the correct placement of the minitracheotomy tube. In addition, oral intubation would have been difficult if not impossible at the time of the respiratory arrest, and would have necessitated emergency tracheostomy in what must have been less than ideal circumstances. Furthermore it is not fully clear how or at what stage the introducer was lost, but a chest X ray performed after each instrumentation of the airway should have led to the early discovery of the misplaced introducer.

The possibility that the introducer could have damaged major intrathoracic or intra-abdominal structures was considered by the thoracic surgeons but the tract was left unexplored as this would have required a major thoracotomy, which was felt to be contraindicated because of the patient's poor respiratory function. Fortunately, no evidence of damage to any major structure emerged in the postoperative period.

Some changes in the technique of minitracheotomy have been suggested in an attempt to reduce the risk of complications. The use of a Seldinger wire technique instead of the minitracheotomy introducer may reduce the incidence of misplacement,[16,17] and a transverse incision close to the cricoid cartilage rather than a vertical incision may reduce the incidence of bleeding.[18]

We feel that the skill and experience of the clinician who inserts the minitracheotomy remains the crucial factor in reducing the risk of complications and suggest that the use of the minitracheotomy should be restricted to those who have had adequate training and supervision in its insertion; in this instance, the experience of the surgeon who inserted the minitracheotomy is not known. In addition, a chest X ray should be mandatory after insertion of a minitracheotomy and any foreign body should be noted and identified as an artefact or a foreign body in the thorax. It may be that these measures will reduce the number of complications of this otherwise useful technique.

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Anaesthesia, 1991, Volume 46, pages 1044–1046

CASE REPORT

A 'postspinal headache' associated with incidental intracranial pathology

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Summary

A 28-year-old woman developed symptoms of raised intracranial pressure associated with an obstructive hydrocephalus following a spinal anaesthetic administered for a Kiellands rotation forceps delivery. A diagnosis of an unverified pineal body tumour was made after computerised axial tomography scanning and the symptoms were effectively treated by the insertion of a ventriculo-peritoneal shunt. This unusual case demonstrates the importance of careful history taking and neurological examination where symptoms of postspinal headache persist.

Key words

Complications; headache.
Anaesthetic techniques, regional; spinal.

Postural puncture headache is a well recognised complication of spinal anaesthesia, particularly in obstetric anaesthetic practice. The incidence of headache is related to the size of the needle puncturing the dura mater, being greatest (70%) following inadvertent puncture with a Tuohy needle[1] and less frequent (< 8%) with the finer 26 and 29 gauge spinal needles.[2,3] The diagnosis is rarely in doubt. The patient complains of severe frontal headache, often accompanied by photophobia, which is worse on standing erect and completely relieved in the recumbent position. The duration of symptoms may vary from 24–48 hours to several days. Cranial nerve palsies may be associated with these symptoms; the abducens nerve is particularly vulnerable when there is a large cerebrospinal fluid (CSF) leak as it becomes stretched across the petrous temporal bone. These palsies, should they occur, may take longer to recover than the headache. Treatment of the symptoms of the headache may initially be conservative, with simple oral analgesia and bed rest, but persistent symptoms may require epidural blood patching, especially in the parturient where mobility is desirable.

This case report illustrates the course of events in a young woman who developed persistent headache, following a spinal anaesthetic, the aetiology of which was subsequently found to be associated with incidental intracranial pathology.

Case history

A 28-year-old woman was admitted to the maternity unit for the birth of her first baby. Labour was complicated by a deep transverse arrest, and a rotational forceps delivery was carried out. A spinal anaesthetic was administered for this procedure and documentation of this indicated no complication. Lumbar puncture had been carried out at the L_{2-3} interspace using a 26 gauge spinal needle with the woman in a sitting position. Hyperbaric bupivacaine 0.5% 2.5 ml was administered which provided satisfactory anaesthesia for the procedure.

In the first 72 hours after delivery, the woman complained of a postdural puncture headache which was treated conservatively with oral analgesia and bed rest. The symptoms subsided and mother and baby were discharged home on the 10th postnatal day.

Three weeks later, her headache recurred suddenly whilst straining at stool. It persisted thereafter for a further 3 weeks before she was admitted, at the request of her general practitioner, for further investigation. In view of the recent spinal anaesthetic, an opinion was sought from a consultant obstetric anaesthetist. On questioning and examination, most of the features of a typical postspinal headache were present. The patient complained of frontal headache, worse on standing erect, accompanied by slight

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photophobia. She also reported diplopia on lateral gaze to the right. She was otherwise well and was apyrexial, exhibiting no signs of meningeal irritation. Neurological examination, including fundoscopy, was normal apart from the presumed abducens nerve palsy. The physicians were advised against a diagnostic lumbar puncture for fear of worsening her symptoms, and the patient was reassured that they were associated with a continuing CSF leak from the spinal puncture and that this would resolve spontaneously. Her headache was improving at the time and it was decided to adopt a 'wait and see' approach to the problem rather than embark upon blood patching. Within 24 hours, her headaches had improved significantly and she was discharged home.

A further 6 weeks elapsed before the general practitioner made contact again with the hospital, this time directly with the anaesthetist, because the headaches had not resolved. The patient was seen the following day as an outpatient in the pain relief clinic and examined by the same anaesthetist. The nature of her symptoms had changed in that the headaches were present when she first woke in the morning, clearing a little towards the end of the day. The relationship to posture was not evident as before. The photophobia had resolved but she continued to complain of diplopia. There were no symptoms or signs of systemic upset and, apart from the headache, she felt perfectly well. Neurological examination was, once again, unremarkable. Urgent referral to the neurology clinic was arranged to exclude incidental intracranial pathology because of the change in nature of her symptoms.

During the following week her symptoms worsened with vomiting accompanying the headaches and admission to hospital under the care of the neurologists was arranged. Examination at the time of this admission showed her to be alert and well orientated. Her headache was exacerbated on flexion of the neck and she displayed some of the features of Parinaud's syndrome; these are a mild retractile nystagmus and pupils reactive to accommodation but not to light. There was no papilloedema and visual fields and acuity were normal. Urgent computerised axial tomography (CT) scanning was carried out and this revealed a tumour in the region of the pineal body with an associated obstructive hydrocephalus. This was treated by the insertion of a ventriculo-peritoneal shunt and, following this, her symptoms completely resolved. Micropathological examination of CSF samples taken at the time of insertion of the shunt revealed no malignant cells.

A debate ensued between surgeons and pathologists regarding further management of this clinical problem, in particular whether biopsy or radiotherapy treatment on an empirical basis was appropriate. Tumour size was monitored by periodical repeat CT scans and, in view of the static nature of the lesion, neither option was pursued. Fourteen months later, the CT scan showed no evidence of the tumour and the possibility was raised that this may have been a proteinaceous arachnoid cyst which had spontaneously drained into the ventricle. The patient was last seen a year later with no evidence of recurrence of the lesion.

Discussion

The pineal body is sited between the splenium of the corpus callosum and the superior colliculi. A tumour in this region will result in drainage obstruction of the third ventricle with a rapid onset of an obstructive internal hydrocephalus. The symptoms and clinical signs of a pineal body tumour will, therefore, include those of raised intracranial pressure and pressure on neighbouring parts of the brain. Pathologically the tumours are mostly teratomas or germinomas and are usually radiosensitive. Pineocytomas are rarer, carry a poor prognosis, and may be associated with hormonal disturbances.[4]

Parinaud's syndrome describes the neurological signs which may be evident due to an expanding lesion in the tectal area. These include defective conjugate ocular deviation upwards, paresis of convergence, ptosis, inequality of the pupils, reflex iridoplegia, corticospinal tract disturbances, nystagmus, ataxia, tremor and sensory loss. Deafness is rarely present.[5]

The case reported raises some interesting points on the question of management. In total, 3 months elapsed from the time of administration of the spinal anaesthetic to the discovery of the true cause of the patient's prolonged symptoms of headache. The question may be asked whether she should have been referred at an earlier stage for a neurological opinion. Would this have expedited the correct treatment? She had certainly developed a spinal headache initially which cleared after 3 days. The reappearance of her symptoms was undoubtedly associated with the internal hydrocephalus. Spinal headaches have, however, been reported to last a considerable period of time if allowed to run their natural course. One case, reported in correspondence,[6] documented a headache which lasted for 6 months following a spinal anaesthetic for fixation of bilateral os calcis fractures and was treated successfully with an epidural blood patch. If a blood patch had been carried out on this woman in the presence of her hydrocephalus, it might have worsened her symptoms rather than improved them. The difficulty lay in distinguishing between neurological signs that may have been attributed purely to a continuing CSF leak (e.g. cranial nerve palsies) and those that were associated with an expanding lesion in the tectal area of the brain. With the subjective complaint of diplopia, it was readily assumed that the problem was simply due to a CSF leak, since there were no other signs associated with raised intra-cranial pressure. Suspicions were only aroused when the patient herself realised that her symptoms of headache were different from those experienced shortly after the spinal anaesthetic.

Another question that arises is whether the lumbar puncture and subsequent CSF leak contributed to the onset of this woman's symptoms associated with her pre-existing pineal body lesion. The alteration of CSF fluid dynamics, with stimulation of increased CSF production, may have hastened the onset of the hydrocephalus. In addition, the reduction of CSF pressure distally, due to the leak in the lumbar region, may have resulted in the lesion acting as a ball valve with subsequent obstruction of drainage from the third ventricle.

Finally, the main lesson to be learnt from this case is that careful neurological assessment is advisable in patients who complain of prolonged headache following a spinal anaesthetic, particularly where there has been initial recovery and then re-emergence of the symptoms. Avoid hasty judgements and reassurances and, as in this case, pressure from a mother who was anxious to go home and look after her baby. In the majority of cases, the problem will be

straightforward but, just occasionally, as with this woman, one may be caught out by something unusual.

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APPARATUS

Variable apparatus deadspace

P. V. SCOTT AND R. P. JONES

Summary

A variable apparatus deadspace was used to maintain normocapnia during artificial ventilation of the lungs in anaesthetised adults. End-tidal carbon dioxide tension could be varied, if the need arose, within the range 4.0–5.2 kPa in both open and circle breathing systems when a fixed tidal volume of 12 ml.kg^{-1} and minute volume ventilation of 120 ml.kg^{-1}.min^{-1} were employed.

Key words

Ventilation; mechanical.
Equipment; deadspace, variable.

'During anaesthesia with paralysis and artificial ventilation, there is a tendency to overventilate which is manifestly safer than underventilation . . . arterial $P\text{CO}_2$ values during anaesthesia with unmonitored artificial ventilation are below normal, often below the apnoeic threshold of $P\text{CO}_2$, and sometimes as low as 2 kPa' [1]. A low arterial $P\text{CO}_2$ is usually allied to a low end-tidal carbon dioxide tension ($P\text{E}'\text{CO}_2$).

$P\text{E}'\text{CO}_2$ may be kept in the normal range by addition of carbon dioxide to the fresh gas flow from a carbon dioxide cylinder attached to the anaesthetic machine; by anaesthesia systems which permit partial rebreathing of mixed expired gas; by hypoventilation of the lungs; or by changes in apparatus deadspace. We have assessed the capacity of a variable apparatus deadspace to maintain normocapnia despite overventilation.

We have taken a low value for normocapnia ($P\text{E}'\text{CO}_2$ 4.9 ± 0.1 kPa). By overventilation we mean hyperventilation of the lungs combined with their hyperinflation, by hyperventilation $P\text{E}'\text{CO}_2$ < 4.8 kPa and by hyperinflation tidal volume > 7.0 ml.kg^{-1} [2].

Patients and methods

Forty-one adults scheduled for major abdominal surgery were studied. Patients known to have lung disease, or who were smokers, were excluded.

Induction of general anaesthesia was standardised to fentanyl 7.0 μg.kg^{-1}, propofol 2 mg.kg^{-1}, and vecuronium 0.15 mg.kg^{-1}. The trachea was intubated and anaesthesia was maintained with nitrous oxide 70% in oxygen, together with halothane 0.5% if indicated. General anaesthesia was supplemented in nine patients with thoracic epidural anaesthesia, in eight with lumbar epidural anaesthesia and in 10 with right-sided interpleural analgesia.

The lungs were ventilated at a positive end-expiratory pressure of 10 cmH_2O (Blease Manley MP4 or Nuffield 400 ventilators, chosen at random). The Manley was used as a minute volume divider (an 'open' system of carbon dioxide elimination) with a measured exhaled tidal volume of 12 ml.kg^{-1} and minute volume of 120 ml.kg^{-1}.min^{-1}. The Nuffield, with the same measured tidal and minute volumes, drove a circle system including carbon dioxide absorption, with vaporizer inside or outside the circle (VIC or VOC) and a fresh gas flow rate of 3 l.min^{-1}.

Monitoring included pulse oximetry (Nellcor 100), capnography, automated oscillometry, electrocardiography, respired concentrations of oxygen and nitrous oxide (Cardiocap, Datex) and halothane (Normac, Datex), delivered concentrations of oxygen (paramagnetic oxygen analyser, Penlon), train-of-four response to peripheral nerve stimulation (Bard), and tidal and minute volume ventilation (Wright's respirometer attached to a heat and moisture exchanger, Fig. 1). The Cardiocap was calibrated before use with a standard mixture of oxygen, carbon dioxide and nitrous oxide and the Normac with standard concentrations of halothane.

The gas mixtures conveyed to and from the patient were continuously sampled from the orotracheal tube connection (Fig. 1). When $P\text{E}'\text{CO}_2$ reached $\leqslant 4.0$ kPa the variable apparatus deadspace described below was used to achieve normocapnia.

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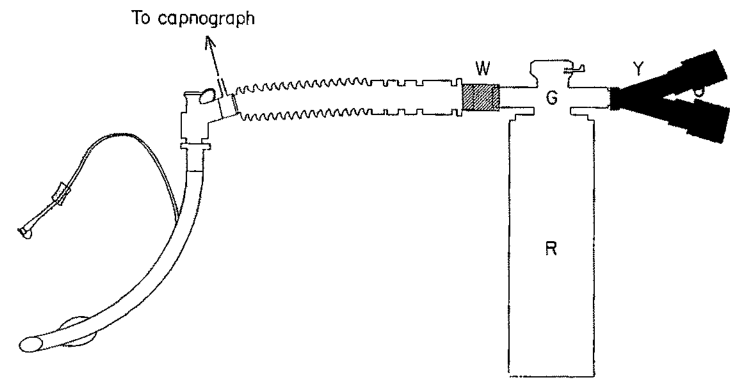

Fig. 1. Placement of variable deadspace reservoir. R = Reservoir; G = Goldman drawover anaesthetic vaporizer; W = Wright's respirometer; Y = Y-piece leading to and from mechanical ventilator. (See text.) Not to scale.

The variable apparatus deadspace

The 70 ml glass chamber was removed from a Goldman drawover anaesthetic vaporizer (Mk 1C, for halothane) and replaced by an 800 ml brass reservoir (the deadspace). The assembly was attached at one end to the respirometer and at the other to the Y-piece of the anaesthesia system (Fig. 1). End-tidal carbon dioxide tension was varied by adjustment of the Goldman vaporizer setting which controlled the proportion of mixed expired gas diverted to and from the reservoir, thus determining the amount of rebreathing (flow splitting: Fig. 2). Apparatus deadspace with the vaporizer setting in the 'off' position (i.e. the 'fixed' deadspace) was 140 ml.

Results

Tables 1 and 2 show the demographic data, duration of anaesthesia, operations performed and systems of anaesthesia.

$P_{E'}CO_2$ reached $\leqslant$ 4.0 kPa in all patients within 15 min of starting mechanical ventilation of the lungs. Thereafter, by adjustment of the variable apparatus deadspace, normocapnia ($P_{E'}CO_2$ 4.9 $\pm$ 0.1 kPa) was always achieved. $P_{E'}CO_2$ could be varied within the range 4.0–5.2 kPa. The maximum $P_{E'}CO_2$ attained (5.6 kPa) was seen in only one patient and on only one occasion. The high value was transient and accompanied by an increase in heart rate and return of the train-of-four response to peripheral nerve stimulation; it decreased to its former value (5.0 kPa) after an incremental dose of vecuronium.

Delivered oxygen concentration was 32 $\pm$ 2%. The lowest recorded inspired oxygen concentration was 28% in 12 patients and the lowest oxyhaemoglobin saturation 96% in three patients.

Table 1. Demographic data and duration of anaesthesia, mean (range).

n	M/F	Age; years	Weight; kg	Duration of anaesthesia; min
41	12/29	56 (22–87)	68 (49–92)	89 (55–180)

Table 2. Surgical operations performed and anaesthesia systems used.

Operations	*n*	Anaesthesia system Open/circle
Cholecystectomy	16	7/9
Hysterectomy	14	8/6
Anterior resection of rectum	4	3/1
Vagotomy and pyloroplasty	3	2/1
Total proctocolectomy	3	2/1
Right hemicolectomy	1	1/0

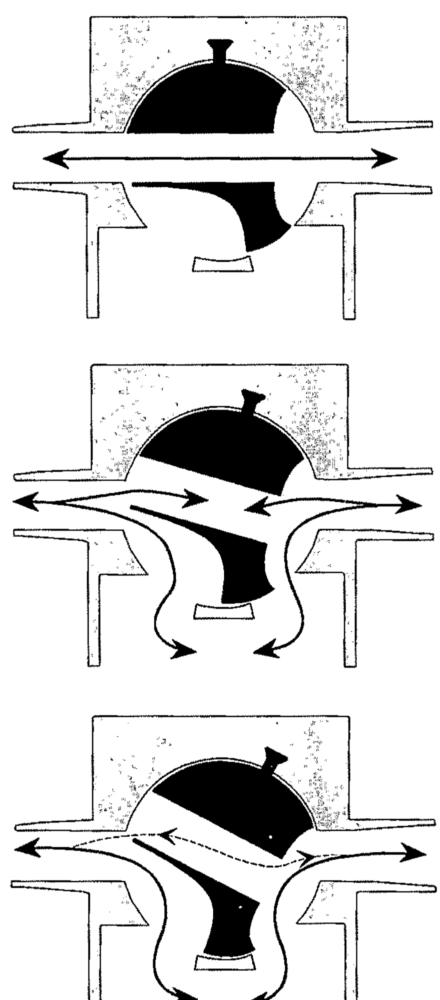

Fig. 2. Schematic diagram to illustrate the principle of a flow splitter. Arrows show directions of flow. Top: closed; centre: half open; bottom: fully open. (Dashed line denotes partial bypass as observed with the Goldman vaporizer; see Discussion.) Not to scale.

Discussion

The aim of the study was to maintain normocapnia in the adult throughout an anaesthetic, despite overventilation of the lungs. This was achieved in all patients in both open and circle systems of general anaesthesia. $P\text{E}'CO_2$ could be varied, if the need arose, in the range 4.0–5.2 kPa at constant tidal volume and minute volume based on a patient's weight.

The soda lime canister in some circle systems can be partly bypassed, so that $P\text{E}'CO_2$ is simply and economically controlled. However, contemporary circle absorbers are either 'on' or 'off'; they have no partial bypass. We used an absorber in the 'on' position. The exclusion of a soda lime bypass may be a retrograde step. It is variously justified by manufacturers as being dictated by European Community recommendations, by the American Food and Drug Administration, and by the International Standards Organisation.

The reservoir, although effective, was inefficient. The potential deadspace was 940 ml and we expected to see a higher maximum $P\text{E}'CO_2$ than 5.6 kPa, a value recorded once only and in one patient only, and which was probably related to the return of muscle tone.

The volume of the reservoir may have been too small; more likely, in the absence of a baffle, there was poor mixing of gases. (In a later model, not reported here, we made a simple baffle which divided the reservoir into halves so that the gas had to pass through the whole of the dead space; the reservoir volume required fell from 800 ml to 580 ml.) The degree of mixing depends on a number of factors, including the flow pattern of the ventilator. A proportion of the gas flow bypassed the reservoir even when the Goldman flow splitter was fully open (Fig. 2). Inefficiency may have been a virtue. Attempts to control $P\text{E}'CO_2$ pose a risk whether carbon dioxide is recycled (endogenous), as in this study, or exogenous [1]. Thus, capnography is essential.

The use of apparatus deadspace to promote normocapnia in the adult without the need to change tidal or minute volume ventilation is a technique long practised in the intensive care unit [2] but rarely in the operating theatre. The concept of a variable apparatus deadspace may appeal to the clinician who adopts a policy of overventilation with open or circle systems of anaesthesia. We do not know how many clinicians adopt that policy; although it has been recommended that anaesthetists should measure ventilation with a spirometer, there is overwhelming evidence that they do not [3, 4]. Nor do we know how many anaesthetists prescribe a pattern of artificial ventilation based on body weight; in one survey, 42.9% of patients had not been weighed [4].

Neither do we know whether overventilation, with or without positive end-expiratory pressure (PEEP), counters the changes in functional residual capacity, pulmonary compliance and closing volumes associated with general anaesthesia [5–9]. Conscious patients in the intensive care unit may become distressed when the lungs are ventilated to normal arterial PO_2 and PCO_2 at a tidal volume of 7 $ml.kg^{-1}$ [2]. Their distress is often relieved by increasing tidal volume to 10–15 $ml.kg^{-1}$. Any fall in $P\text{E}'CO_2$ may be corrected by adding apparatus deadspace. Large tidal volumes and large minute volume ventilation also seem to improve arterial PO_2 in patients with respiratory failure; whether they improve oxygen flux is debatable.

One of the principal objects of modern anaesthesia is to prevent pain during and after surgery with the minimum effect on homeostasis. The optimum oxygen flux is desirable. Overventilation increases arterial PO_2 and arterial oxygen content, but large tidal and minute volumes during anaesthesia do not improve oxygen flux because they reduce cardiac output [10]. However, in the presence of overventilation, normocapnia is more likely than hypocapnia to preserve homeostasis in respect of cardiac output [10], cerebral blood flow, P_{50}, arterial pH, and intracellular pH (including cerebral cell pH). Further, 'inhalation anaesthetics abolish the peripheral chemoreceptor ventilatory drive and have a profound effect even at 0.1 MAC. The use of high concentrations of oxygen at the end of anaesthesia also suppresses peripheral chemoreceptor drive. Thus a hypocapnic patient may be totally devoid of chemoreceptor drive at the end of a period of anaesthesia with artificial ventilation' [1].

We have demonstrated that the apparatus which we have described offers a convenient method of controlling $P\text{E}'CO_2$ during hyperventilation, and overcomes concerns about the hazards of carbon dioxide cylinders on anaesthetic apparatus [1]. Whether normocapnia offers advantages in the presence of hyperventilation requires further investigation.

Acknowledgments

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APPARATUS

Continuous direct and indirect blood pressure measurement (Finapres) in the critically ill

I. K. FARQUHAR

Summary

Continuous noninvasive blood pressure measurement is of great potential use in the critically ill. This study was designed to find out whether measurements of blood pressure by a Finapres accurately represented intra-arterial pressure. Comparisons were made between readings from a radial artery line and from a Finapres finger cuff in 10 critically ill patients. There was an unpredictable but usually stable difference between measurements from the two sources; this difference varied in magnitude and direction in individual patients. At present the Finapres cannot be recommended as a substitute for intra-arterial blood pressure measurement in the critically ill.

Key words

Measurement techniques; plethysmography.
Equipment; Finapres.

Modern noninvasive blood pressure measurement devices allow frequent estimation of blood pressure without operator intervention. This frees the clinician to concentrate to a greater extent on other observations and therapy. However, the maximum frequency with which readings may be obtained is four per minute and then only for a limited period of 5 minutes (the normal maximum frequency is once per minute). It would be an advantage if noninvasive blood pressure could be measured continuously, in a fashion analogous to direct blood pressure measurement. This would allow immediate detection of changes.

A device which measures blood pressure noninvasively on a continuous basis from a finger cuff, the Finapres, has now been available for some time.

Description of Finapres

The Finapres is based on the 'volume clamp' principle of Peñaz.[1] The blood volume of the finger varies in a cyclical fashion with each cardiac cycle because of the attendant variation in systemic pressure. This variation is detectable by a photoplethysmograph attached to a finger and a display of this type is seen in many of the pulse oximeters in use today. If a pneumatic finger cuff can be inflated and deflated rapidly enough to maintain a constant finger blood volume (and thus photoplethysmographic signal) then the arterial wall will have been 'unloaded'. In other words, there will be a state of zero transmural pressure. In this situation (given that there is no significant pressure attenuation in the intervening tissues) the cuff pressure must equal intra-arterial pressure (IAP). A 'real time' display of the cuff pressure should therefore be equivalent to a display of the intra-arterial pressure waveform of the digit and analysis of the cuff waveform would allow measurement of systolic and diastolic pressures and calculation of a 'true' (area under the curve) mean blood pressure. This principle has been embodied, after considerable research, in the Finapres (Ohmeda).

The Finapres consists of a central monitoring unit which comprises a control panel and display, monitoring electronics and an air pump to supply the finger cuff. This main unit is connected by a cable (containing electronic cabling and an air line) to a secondary unit which is attached to the subject's wrist by a 'Velcro' strap. The secondary unit contains a pressure transducer, a rapid-acting servo and valve, which together control the cuff pressure. The unit is connected to a pneumatic finger cuff which contains a sensing system for the photoplethysmograph. This comprises a light-emitting diode (LED) emitter and its receiver in a similar configuration to that found in an oximeter (with the exception that the light path is coronal rather than sagittal). The air pump in the main unit delivers air at a constant pressure and the proportion of this pressure delivered to the cuff is determined by the servo and valve. The photoplethysmograph signal is linked to the

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servo/valve system in a negative feedback arrangement. Thus, if the photoplethysmograph signal increases, cuff pressure is increased so as to return the signal to its previous value.

The Finapres functions in the following fashion. When the device is switched on, a self-diagnostic procedure is run. Upon starting the measurement sequence, the cuff pressure is increased in a stepwise fashion to a suprasystolic level and then back to zero. The point of maximum variation in the photoplethysmograph signal is taken as a set point and the pressure in the cuff is then varied in a cyclical fashion in order to maintain a steady photoplethysmographic signal strength. Because changes in arterial wall tone may affect the reading from the device, the Finapres undergoes a brief recalibration every 70 cardiac cycles.

The device displays a pressure waveform in 'real time' with a digital display of systolic, diastolic and mean blood pressures averaged over three cardiac cycles. There is an additional blood pressure trend display with a variable time axis. Such a system has obvious attractions in anaesthesia and intensive care especially in patients in whom blood pressure monitoring is required on a beat-to-beat basis but in whom blood gas analysis is not necessary, or as a temporary measure in haemodynamically unstable patients in the period before placement of an intra-arterial line. In order to investigate the feasibility of using the Finapres in such a role it was decided to compare blood pressure measurements derived from the Finapres and from an intra-arterial line in mechanically ventilated patients on the intensive care unit.

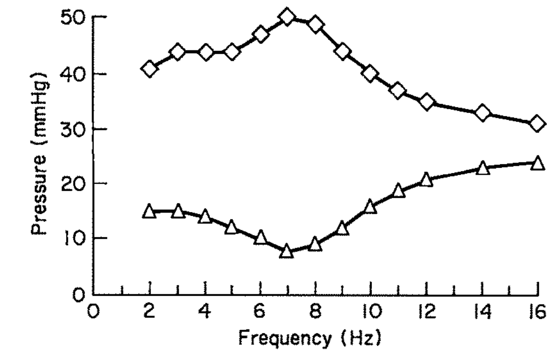

Fig. 1. Representative plot of maximum and minimum pressures recorded by a standard intra-arterial pressure measurement system driven by a sine wave of varying frequency, showing a natural frequency of approximately 7 Hz.

Methods

Permission to undertake the study was obtained from the Ethics Committee of the hospital and consent to study patients was obtained from their next of kin. Ten consecutive patients on the Adult Intensive Care Unit of the University Hospital Nottingham, who were not severely haemodynamically unstable, were studied (Table 1). A 20 g 'Abbocath' cannula was placed in a radial artery, and attached to a standard intensive care flushing system (British Viggo) and transducer connected to a Simonsen and Weel Triscope system. The natural frequency of two standard intra-arterial monitoring systems (including a cannula) was investigated by application of a sinusoidal pressure wave to the system at varying frequencies (Fig. 1) and all those used in the study were examined by a 'flush test';[2] the latter also allowed estimation of the damping coefficient (ζ) of the system.

The intra-arterial system was flushed and checked for any air bubbles, which were cleared if present. The intra-arterial and Finapres pressure (FP) transducers were then calibrated against a mercury manometer. The finger cuff was applied to the index finger of the ipsilateral hand of the arm in which the arterial cannula had been placed and Finapres measurement was started. Analogue signals from both the Finapres and the intra-arterial monitor were recorded on an FM tape recorder. The calibration voltages from the intra-arterial pressure transducer were recorded on tape at the start of the session as was a calibration voltage from the Finapres, equivalent to a pressure of 100 mmHg. Once the Finapres had been making measurements for at least 2 minutes, data logging on the FM tape recorder was started. Data were recorded from each patient for at least 5 minutes.

The signals from the tape were later processed through a 'MacLab' analogue-to-digital converter into an Apple Macintosh SE microcomputer, sampling each channel at a frequency of 100 Hz. Data were obtained from 200 consecutive pairs of cardiac cycles from each patient's records. This gave readings of systolic, diastolic and mean pressures for each device. These readings were then analysed by the graphical method described by Bland and Altman for the comparison of two measuring devices, one of which is held to be the standard.[3] Briefly, this technique requires the plotting of information derived from pairs of data points, one from each measurement device. The mean of the two values is plotted against their difference. The 'limits of agreement' are defined as the mean difference ± 2 standard deviations of the mean. If the magnitude of the 'limits of agreement' is deemed to be clinically significant then the new method of measurement may not be substituted for the old.

Table 1. Details of patients studied.

Patient	Age	Diagnosis
1	22	Multiple trauma, fat embolism
2	34	Head injury, facial fractures
3	75	Exacerbation of chronic obstructive airways disease
4	27	Multiple trauma
5	55	Postoperative bronchopneumonia
6	67	Multiple rib fractures
7	44	Head injury
8	18	Head injury
9	19	Head injury, rib fractures
10	65	Postneurosurgery

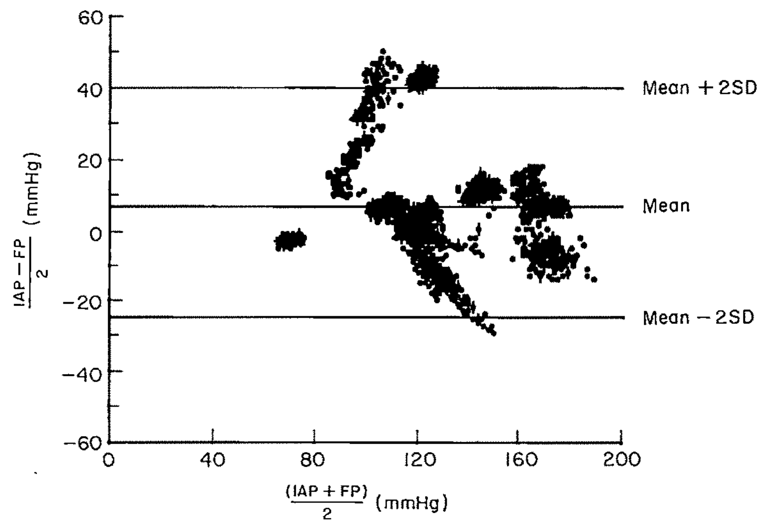

Fig. 2. Plot of data for systolic pressure for all patients (200 points per patient). IAP, intra-arterial pressure; FP, pressure measured by Finapres.

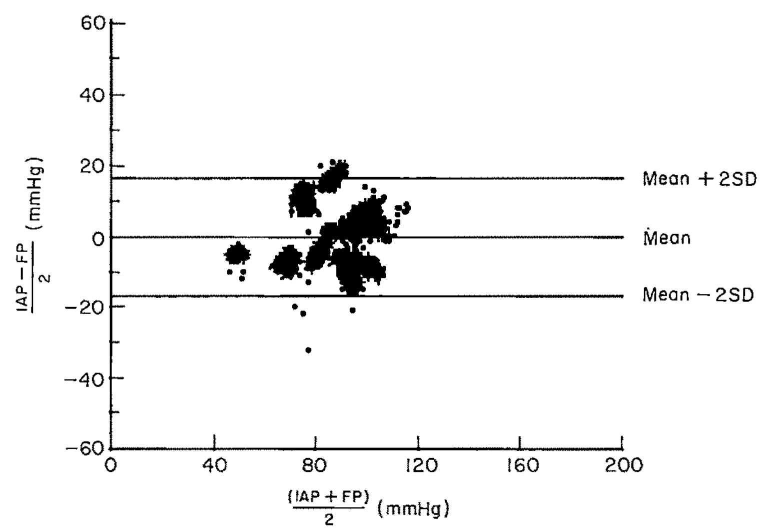

Fig. 3. Plot of data for mean pressure for all patients (200 points per patient).

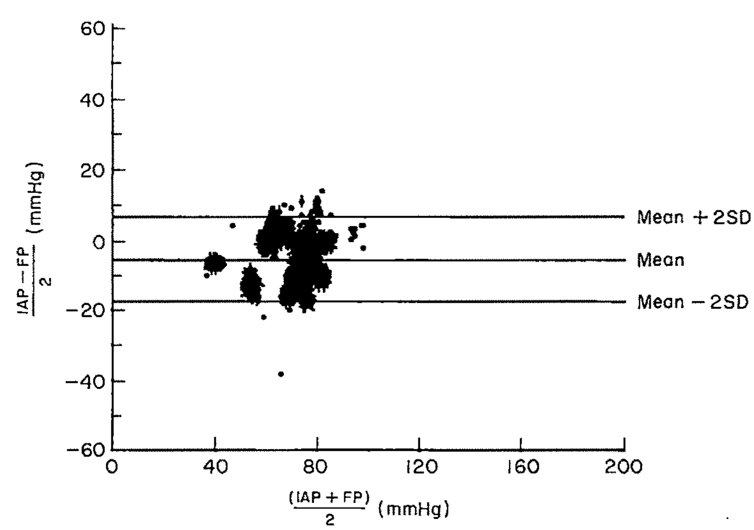

Fig. 4. Plot of data for diastolic pressure for all patients (200 points per patient).

Table 2. Mean discrepancies in mmHg, (IAP–FP) and SD for individual patients.

	Systolic BP		Diastolic BP		Mean BP	
	IAP–FP	SD	IAP–FP	SD	IAP–FP	SD
Patient 1	7.9	3.3	−12.2	3.3	−9.2	2.3
Patient 2	−2.7	0.6	−6.4	1.0	−5.0	1.0
Patient 3	10.9	2.8	−1.2	1.9	5.7	2.0
Patient 4	6.2	1.4	−14.5	2.3	−5.1	2.2
Patient 5	2.8	3.0	−12.6	2.9	−7.1	3.0
Patient 6	−1.8	1.5	0.4	1.5	1.1	1.5
Patient 7	−6.6	3.1	−1.5	4.8	3.6	2.9
Patient 8	28.8	11.7	0.7	2.9	10.4	2.2
Patient 9	−13.8	5.4	−9.5	1.6	−7.3	2.2
Patient 10	42.6	1.6	2.2	1.5	16.4	1.6

Results

The natural frequencies of the two arterial line systems subjected to sine wave oscillation were 7 and 9 Hz respectively. The mean natural frequency of the systems used in the study was 14 Hz (SD 5.6) and the damping coefficient (ζ) was 0.57 (SD 0.3).

The results for systolic, diastolic and mean blood pressures for the 10 patients studied are displayed in Figures 2, 3, and 4 respectively. Two hundred data points are plotted for each patient. The mean differences between the devices (IAP–FP) were as follows (pooled data): systolic 7.45 (SD 16.3), mean −0.31 (SD 8.5) and diastolic −5.79 (SD 6.6). This results in limits of agreement ranges of 65.2 mmHg, 34 mmHg and 26.4 mmHg respectively. Table 2 shows data for the individual patients.

Discussion

It is clear that there were considerable differences between readings from the Finapres and the intra-arterial pressure line. Although the mean differences between the two methods are relatively small, the limits of agreement (mean ± 2 standard deviations) are wide. Therefore little confidence can be put in the relationship between IAP and FP in any individual patient. However, it is also apparent from the clustering of data points that the relationship between the two measurements is stable for individual patients. This impression is confirmed by the data in Table 2. This shows that the SD of the difference between IAP and FP in individual patients is small. Therefore, the Finapres follows trends in blood pressure accurately. However, it should be noted that there are data in the systolic pressure plot which suggest a shift in the relationship between IAP and FP in two patients.

There may be a number of reasons for the discrepancies which relate either to the intra-arterial system or to the Finapres (Table 3).

The standard intensive care arterial line system in this study had a natural frequency of 14 Hz. This is lower than the recommended factor of 10 above the fundamental frequency suggested to be necessary for faithful reproduction of the arterial waveform.[4] In other words, in order faithfully to reproduce an arterial waveform at a heart rate of 120 beats/minute (2 Hz), the fundamental frequency of the system should be greater than 20 Hz. However the damping factor of 0.57 places the system used in the study just within the response range suggested by Gardner.[2] The problem of arterial line systems with low fundamental frequencies is illustrated in Figure 1. As the frequency applied approaches the natural frequency of the system there is an increase in the maximum pressure and a decrease in the minimum pressure registered. However, an effect of this kind is not apparent in the results which show only a slight positive offset for intra-arterial systolic pressure–Finapres systolic pressure, with a wide spread of values both above and below this mean.

It is possible that the intra-arterial cannula may have been 'kinked' in some cases, thus affecting the response of the intra-arterial system. Unfortunately it is not possible to assess the damping of an intra-arterial system by examining the waveform,[2] because of the wide variability in the character of faithfully reproduced normal waveforms.

The two systems measure pressure at different sites within the arterial tree. It would be expected that the systolic pressure would be slightly higher in the digital arteries than in the radial artery and that both the mean and diastolic pressures would be slightly lower. This complex phenomenon is said to be related predominantly to reflections of the pulse wave by the periphery of the circulation.[5] This leads to positive interference between the anterograde and retrograde waveforms in the more peripheral arteries, to a 'peaked' waveform and to a systolic pressure that increases from central circulation to the periphery. However, this 'peaked' shape has a smaller area-under-the-curve, i.e. mean blood pressure, than waveforms from the aorta and thus the mean blood pressure declines progressively from the central to the peripheral circulation.

The methods of pressure measurement are different. The Finapres measures the cuff pressure and not blood pressure and the underlying assumption is that there is a 1:1 relationship between cuff and digital artery pressure. The fact that the Finapres recalibrates itself every 70 cardiac cycles suggests that this relationship is not stable and it is the author's observation that despite this recalibration there may be a drift with time in the relationship between intra-arterial and Finapres pressures.

Table 3. Possible causes of discrepancies between methods.

Arterial line system characteristics
Kinking of arterial cannula
Pressures measured at different sites in arterial tree
Pressures measured by different methods
Presence of arterial cannula affecting distal pressures
Kinetic effect of pulsatile flow
Peripheral vasoconstriction
Release of vasoactive metabolites from arterial endothelium

Table 4. Summary of published data. All figures are mean (SD) for IAP–FP unless otherwise indicated.

Systolic	Mean	Diastolic	Reference
1 (9.6)	9 (6.8)	4 (6.1)	11
	−0.8 (5.4)		12
7 (14)*	1 (10)*	−3 (9)*	13
−5 (8)	6 (5)	6 (4)	17
3.9 (21.6)†	−2.9 (14.3)†	1.3 (15.5)†	15
−1.2 (5.4)		−2.9 (5)	16
−1.9 (10.6)	3.7 (8.3)	3.2 (7.2)	14

*Standard error of the mean.
†Calculated from reported data.

A decision was made to monitor blood pressure by both methods in the same arm; however, it is possible that the presence of the radial artery cannula proximal to the Finapres cuff may have altered the digital artery pressure. Kurki *et al.*[6] showed that there was only a brief effect of radial artery cannulation on blood flow velocity measured by Doppler and that the Doppler values returned to within 10% of normal within a maximum of 17 minutes; they suggested that the Finapres 'lost adequate signals' only when blood flow velocity decreased by $\geqslant 65\%$.[6] However, this work did not address the effect of chronic radial artery cannulation on distal blood flow velocity.

All radial cannulae were directed proximally. In these circumstances the blood pressure measured included a contribution from the kinetic energy of the blood flow. This will tend to exaggerate intra-arterial blood pressure.[7]

Peripheral vasoconstriction has been shown to affect Finapres readings[8,9] and since the patient's peripheral circulation was not examined for vasoconstriction it may, if present, have contributed to the discrepancies between the two measurement methods.

Finally the potent effects of endothelium-derived relaxant factor (EDRF, almost certainly nitric oxide) have been documented.[10] The half-life of EDRF is so short as to render it undetectable in blood, but it is possible that the presence of a cannula within the lumen of the radial artery may have effects on distal arterial tone by stimulating the release of other locally acting vasoactive substances.

It is therefore apparent that there are a number of difficulties in interpreting both IAP and FP. However, if IAP measurement is taken as the 'gold standard' the present study shows that the Finapres represents IAP inaccurately in individual critically ill but haemodynamically stable patients. These results are in agreement with studies in other types of subject[11–17] (Table 4). The small inter-method differences and standard deviations noted in the study by Parati *et al.*[16] may be due to the fact that data were averaged over varying time periods in the analysis, thus reducing variability. Comparisons between studies are complicated by the fact that some do not cite the natural frequency or damping factor of the IAP measurement systems used.[12,13,15,16,18] One study lists the natural frequency only.[11] The two studies that give both parameters[14,17] include a range of values that suggest that the performance of some of the IAP systems used would be unsatisfactory by Gardner's criteria.[2] These difficulties are compounded by the different analyses used.

However, despite the fact that the Finapres cannot be used as a substitute for an intra-arterial line in individual patients it may be valuable in research. Analysis of pooled data from this study show that there is little difference between IAP and FP for patient groups. Therefore the Finapres may be used as a research tool as a substitute for an IAP monitor, provided that only pooled data from the experimental groups are used for analysis. In addition, the present study shows that the Finapres detects changes in IAP extremely accurately and may therefore be used in individuals, provided that only changes from a baseline FP are used for analysis.

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Anaesthesia, 1991, Volume 46, pages 1056–1058

Forum

The impact of the appearance of the anaesthetist on the patient's perception of the pre-operative visit

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Summary

The clinician's appearance is often considered a symbol which identifies and defines specific characteristics of the individual. Opinion of both lay and medical personnel on appropriate clothing inclines towards formal dress. Our aim was to assess the effect of the anaesthetist's appearance during a ward visit on the patient's evaluation of either the visit or the anesthetist himself. In our sample of 66 patients we found no evidence that the style of dress (formal: suit and tie, informal: jeans and open-necked shirt) affected that evaluation. However, when 138 patients were asked to rate the desirability of items of clothing for a male hospital doctor they expressed a preference for traditional clothing; a suit was rated as desirable and jeans as one of the four most undesirable items. We conclude that despite the conservatism of expressed opinions, the clothing worn by the anaesthetist is irrelevant to the patient's satisfaction with the visit.

Key words

Anaesthetists; appearance.

A hospital stay is often a stressful event, and patient anxiety may be heightened particularly before surgery [1]. The pre-operative visit by the anaesthetist to surgical patients provides an opportunity to brief them about the forthcoming procedure, and also presents a chance for the patient to seek information and possibly reassurance about the processes involved. This visit has been shown to reduce anxiety on the day of the operation [2]. The importance of facilitating this communication is self-evident, and all factors which may affect it should be considered.

Communication is a vital and complex component of the clinician–patient relationship, and that communication includes verbal and nonverbal messages. An ever-present part of nonverbal communication is appearance. The clinician's appearance is often considered an important symbol which not only identifies the individual as a clinician but also defines specific characteristics. Furthermore, certain assumptions are commonly made about what constitutes appropriate dress.

Clinician appearance has been a topic of interest since Hippocrates argued that the clinician should 'be clean in person, well-dressed, and anointed with sweet-smelling unguents' [3]. The significance of the doctor's white coat as part of the image of the physician has been considered a symbol of both authority and of a supernatural power [4]. However, recent research has indicated that the rationale behind the wearing of the white coat is more pragmatic; the three main reasons cited were ease of recognition, useful pockets and protection of ordinary clothes [5]. An examination of the images of medical professionals, as presented in advertisements in the trade press, has demonstrated that these reflect the dominant social themes. Over the last 20 years the image of the doctor has moved away from the white coat and stethoscope towards an image of science in action and high technology [6].

Few studies have sought to investigate the patient's perception of the clinician's clothing. A survey of the attitudes expressed by both patients and clinicians to selected items of a doctor's appearance showed that whilst patients were, on balance, less discriminating in their selection than were the clinicians, they tended to favour more traditional items [7]. Another survey produced a similar result but also showed that junior doctors tended to dress more informally than patients had indicated was appropriate [8]. When patients were asked to assess a physician's competence from studying pairs of photographs there was a marked tendency to be more prepared to ascribe competence to those who were dressed formally (in a laboratory coat). However, this method demands a qualitative inference from appearance alone, which cannot be said to reflect real life [9].

A study in which adolescents were asked to evaluate their visit to a general practitioner showed that the dress style of the physician did not influence their attitude to him [10]. Furthermore, a recent paper has shown that although a general practitioner's patients noticed and recalled their doctor's clothing they listed appearance as unimportant. There was also some evidence that patients tended to prefer their general practitioner to wear casual clothes [11].

Whilst a certain standard of appearance is customarily assumed to be required of hospital doctors, no data have been published which assess the way in which the appearance of the doctor visiting the ward affects the patient's response to that visit. This study was designed to examine this issue and to discover whether British patients' attitudes

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to the doctor's appearance were the same as those expressed by American patients [7]. Study 1 assessed the impact of a male anaesthetist's clothing on the patient's assessment of the pre-operative visit and Study 2 examined patients' expressed attitudes about appropriate clothing for a male hospital doctor. The gender of the doctor was kept constant in both studies, partly to reduce variability and partly because orthodox standards of female dress are less easy to define.

Methods

Study 1. Inpatients were visited routinely by an anaesthetist before the operation. The anaesthetist wore a suit and tie when he visited half the patients (formal group), and denim jeans and an open-neck shirt when he visited the remainder (casual group). The clothing was always clean and his general appearance was well-groomed. In neither case was he wearing a white coat. Within a time interval of no more than 15 min the patient was approached by a researcher who introduced himself and invited the patient to participate in a survey of patients' views of the doctor's ward visits. It was explained that this interview was in confidence and no names were requested. The only details noted were the sex and age of the patient. The interview schedule used two multiple affect adjectival check-lists (MAACL) to measure the patient's responses to the visit and to the anaesthetist. MAACL is a technique used to assess attitudes. The individual is presented with a series of adjectives which might apply to the object of interest. They are then requested to select those adjectives which they consider applicable and reject those which seem inappropriate. In the present study the two checklists comprised a set of 21 and 27 adjectives respectively, and the patient was asked to select those which accurately described their assessment of, first, the visit and then the anaesthetist. A score was derived from this technique: one point for each positive adjective selected and one for each negative rejected [12]. At no point was the appearance of the anaesthetist mentioned. The difference in rating score between the groups was assessed with a Mann–Whitney *U*-test, and Chi-squared tests were used to assess the associations between group and individual adjectives of interest.

Study 2. Patients were approached by a researcher who introduced himself and asked if they would like to participate in a survey, again assuring confidentiality and anonymity. The interview schedule comprised a list of items of appearance, and patients were asked to rate these as 'desirable', 'neutral' or 'undesirable' for a hospital doctor on a ward visit. Chi-squared or Fisher's exact tests, as dictated by the expected frequencies, were used to test evidence of association between groups and responses.

Results

Study 1. Data were collected from 35 female (mean age 46, range 18–77 yr) and 31 male patients (mean age 52, range 18–81 yr). All the positive adjectives to describe the pre-operative visit were selected by at least 80% of patients; the most frequently selected adjective was pleasant. Seven of the negative adjectives were not selected by any patient. The responses of the two groups of patients were similar (Table 1). However, fewer patients in the formal than in the casual group described the visit as 'useful' or 'informative' and significantly fewer described it as 'calming' ($p < 0.02$). All the positive adjectives to describe the anaesthetist were selected by a minimum of 60% of the patients, with 'friendly' being selected most frequently. Seven of the negative adjectives were not selected by any patient, and the responses of the two groups of patients were similar (Table 2). There was no difference in the rating score of either the visit or the anaesthetist between those in the formal and those in the casual group. There was no evidence that these scores were affected by either the age or sex of the patient.

Study 2. Data were collected from 70 female (mean age 46, range 18–89 yr) and 68 male patients (mean age 54, range 18–86 yr). The ratings of items on the check-list were assigned a mean score in the same manner as that employed by Gjerdingen *et al.* [7] (calculated from a three-point scale where 1 is desirable, 2 neutral and 3 undesirable) in order to compare the results from the two studies (Table 3). The items rated as desirable by the greatest number of patients were name-tag and white coat. Those items considered undesirable by the greatest number were jeans, long hair, earrings and clogs. A comparison of the two studies shows the order of ratings to be similar between samples, but in the present study the range of scores was greater than in the American study, suggesting a greater

Table 1. Descriptions of pre-operative visit.

Group	Casual $n=33$	Formal $n=33$	Total $n=66$
Pleasant	32	31	63
Relaxed	32	30	62
Helpful	31	31	62
Reassuring	31	30	61
Calming	33	27	60
Encouraging	31	29	60
Comforting	28	29	57
Useful	31	26	57
Informative	31	25	56
Satisfactory	26	27	53
Impersonal	2	1	3
Disappointing	1	—	1
Tense	—	1	1
Worrying	1	—	1
(not selected: useless, unhelpful, unpleasant, unsatisfactory, confusing, disturbing, awkward.)			
Rating score, mean (SD)	20.2 (1.3)	19.6 (2.1)	

Table 2. Descriptions of the anaesthetist.

Adjective	Casual	Formal	Total
Friendly	32	33	65
Capable	32	31	63
Confident	31	32	63
Professional	31	31	62
Hurried	31	32	63
Helpful	29	32	61
Polite	31	30	61
Competent	31	30	61
Approachable	31	30	61
Caring	29	30	59
Kindly	28	28	56
Patient	26	30	56
Warm	26	26	52
Unhurried	23	19	42
Distant	2	1	3
Cold	2	—	2
Impersonal	—	1	1
Inexperienced	—	1	1
Uncertain	—	1	1
Nervous	1	—	1
(not selected: unsure, unhelpful, arrogant, rude, stand-offish, impatient, impolite)			
Rating score, mean (SD)	25.3 (2.1)	25.4 (2.2)	

Table 3. Patients' rating of items of doctor's appearance.

Item of dress	Mean rating	
	Present study	Gjerdingen *et al.* [7]
Name tag	1.1	1.3
White coat	1.2	1.5
Polished shoes	1.4	1.5
Short hair	1.4	1.4
Tie	1.5	1.7
Suit	1.8	2.0
Aftershave	2.0	1.9
Corduroy trousers	2.3	1.9
Open-neck shirt	2.4	2.1
Sandals	2.6	2.5
Trainers	2.7	2.4
Jeans	2.7	2.3
Long hair	2.7	2.5
Earring	2.8	2.5
Clogs	2.8	2.6

Means are calculated from a three point scale where 1 is desirable, 2 neutral and 3 undesirable.

consensus on desirability and undesirability. The distribution of responses between male and female patients was very similar. However, there was a significant association between the age group of the respondents and the type of responses. Patients over 60 years of age were significantly more likely than those under 60 years to describe as desirable a tie, a white coat and short hair ($p < 0.05$) and a suit ($p < 0.01$). They were also significantly more likely to describe as undesirable long hair ($p < 0.05$) and corduroy trousers ($p < 0.01$). Thirty-nine patients took part in both studies and separate analyses were performed on their responses to the items. Of the 16 patients in the casual group seven described jeans as undesirable compared with 21 of the 23 in the formal group ($p < 0.005$). Only one patient in the casual group described a suit as desirable compared with 14 in the formal group ($p < 0.005$). This response, for both groups in turn, was compared with that of the rest of the sample, and whilst no association between group and response was found for the casual group there was a significant association for the formal group ($p < 0.0001$).

Discussion

It would seem that if an anaesthetist wears clean casual clothing it will not have a detrimental effect on the way in which the patient assesses either the pre-operative visit or the anaesthetist himself. However, if patients' opinions on a hospital doctor's clothing are sought, there is an expressed preference for formal clothing, and jeans are one of the most 'undesirable' items. This finding highlights the problems and dangers of extrapolating from professed opinions. A study which showed that patients rated traditional items of appearance more positively concluded that this confirmed 'the importance of the physician's appearance in physician–patient communication' [7]. The present results show that this is not the case. It is known from psychological literature that expressed attitudes will not necessarily predict behaviour [13].

It is noteworthy that the items which were described as desirable by most people were those which identify the physician: the name-tag, and the white coat. This appears to be more pertinent for inpatients than the style of clothing worn.

It is apparent that there was an effect of the anaesthetist's visit on the responses to the items in the checklist. There was no evidence to suggest that those who had been visited by a doctor wearing jeans were likely to respond differently to that item from those who had not been visited as part of the study. However, it seems that those who were visited by a doctor in a suit did respond more positively to this item; the trend towards an approval of traditional dress seems to have been augmented. It is not possible to know whether such a change would be conscious or preconscious.

It seems reasonable to conclude that there is a standard image of appropriate traditional clothing for hospital doctors, as shown by the responses to the list of items. However, the clothing worn does not seem to affect the way in which patients respond to the pre-operative visit.

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Guided isoflurane injection in a totally closed circuit

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Summary

Twenty-six patients undergoing middle ear surgery were anaesthetised using a completely closed circuit into which liquid isoflurane was injected using a syringe pump. The injection rate was guided by a table of calculated rates of isoflurane uptake, utilising the square root of time principle, at succeeding time intervals in different weight groups. A constant alveolar concentration of 1.3 MAC was aimed for. The injection rate was changed to that for the higher or lower weight group appropriate to the time interval whenever clinical signs indicated inappropriate depth of anaesthesia. A mean of 10.3 ml liquid isoflurane was used to maintain anaesthesia for a mean of 82.3 minutes. Blood pressure was maintained at 75% of the pre-operative value. Mean arterial blood gas data and changes in plasma catecholamine levels were within the normal range. The mean recovery time was 10.5 minutes. Syringe pump delivery of liquid isoflurane avoided fluctuations that result from bolus injections of unit dose. The implemented injection rate table, working as a therapeutic window, guided redosing, reduced calculation time and served as a record. The technique is safe, economic and adaptable to variations in uptake and response to inhalational anaesthetics.

Key words

Equipment, breathing systems; closed.
Drugs; isoflurane.

Isoflurane has a wide circulatory margin of safety compared with other halogenated agents, but its synthesis and purification is complex and expensive.[1] Its resistance to biodegradation may explain the minimal or absent adverse effects on the liver and kidney.[2] Cost considerations and increased concern about the effects of escaping anaesthetics on operating room staff and the environment has redirected attention to the closed circuit technique. Useful work in this respect has been carried out, including the use of a closed-loop servo-mechanism to control liquid isoflurane injection into a closed-circuit breathing system based on the concept of MAC.[3–5] However, the desired alveolar concentrations were modified whenever evaluation of the clinical signs indicated inappropriate depth of anaesthesia, since there is no reliable means of quantifying depth of anaesthesia for the control of anaesthetic delivery. The added instruments (anaesthetic gas monitor and closed-loop control system) will increase the complexity and expense of the system and are liable to signal error effects.[5]

This paper describes a simple and clinically feasible technique for a closed circuit liquid isoflurane injection utilising the principle of Lowe and Ernst,[6] but provides flexibility to deal with variations in uptake and response to anaesthesia.

Patients and methods

Principle. The use of a totally closed circuit requires knowledge of the actual uptake of anaesthetic vapour by the patient. Based on the work of Lowe and Ernst in 1981,[6] inhalational anaesthetics are taken up by the whole body as a function of the square root of time. The dose of anaesthetic required to fill the ventilatory and arterial transport system with the desired concentration is the prime dose. It is introduced once for each case and the resultant alveolar concentration is maintained by fixed unit dose given at times equal to the squares of the natural numbers to compensate for uptake by the tissues i.e. at the 1st, 4th, 9th, 16th minute etc.[6] Calculation of these doses, for 1.3 MAC for various body weights gives the prime and unit doses in Table 1.

Using a syringe pump, the prime dose together with two unit doses were injected into the closed circuit during the first 4 minutes of anaesthesia i.e. during the first two time intervals. Thereafter, a unit dose was planned to be given during each subsequent time interval. The rates of liquid isoflurane injected into the circuit during the first two and each of the subsequent time intervals were calculated for different weight groups (Table 1). A copy of this table was included with the anaesthesia record of each patient before the operation.

Doses were for standard patients, calculated to have 15% adipose tissue. In the obese patient, adipose tissue exceeding this percentage should be subtracted from the total body weight before assigning the patient to a weight group in Table 1.[6] The total body fat can be estimated using Gubner's equation:[7] fat % $= 90-2$ (height to girth); height and waist-girth are recorded in inches.

Circuit. The circuit used (Ohio Model 21) was connected to an upright bellows ventilator (Ohmeda 7000). The end-tidal bellows position was a constant visual check that the circuit volume was being maintained. The oxygen fraction was monitored at the expiratory limb of the circuit ($F\text{E}O_2$) using the Ohmeda 5100 polarographic oxygen analyser. Figure 1 shows the schematic arrangement of the circuit components.

To test for leaks, the circuit was connected to the ventilator, the pop-off valve closed, and patient Y-piece fitted with a test lung. The ventilator reservoir bellows was filled to the 200 ml spirometer mark and oxygen flow was then closed. With the respiratory rate set at 10/minute and minute volume at the minimum, the ventilator was turned

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Table 1. Rate of liquid isoflurane injection in closed circuit (ml/hour).

Time interval (minutes)			4	5	7	9	11	13	15	17	19	21	23
Elapsed time (minutes)			0–4	4–9	9–16	16–25	25–36	36–49	49–64	64–81	81–100	100–121	121–144
Weight group (kg)	Prime dose (ml)	Unit dose (ml)											
30–39	1.14	0.63	36.0	07.5	05.4	04.2	3.4	2.9	2.5	2.2	2.0	1.8	1.6
40–49	1.21	0.78	41.6	09.4	06.7	05.2	4.3	3.6	3.1	2.8	2.5	2.2	2.0
50–59	1.28	0.93	47.1	11.1	08.0	06.2	5.1	4.3	3.7	3.3	2.9	2.7	2.4
60–69	1.35	1.06	52.1	12.9	09.1	07.1	5.8	4.9	4.2	3.7	3.3	3.0	2.8
70–79	1.41	1.19	56.9	14.3	10.2	07.9	6.5	5.5	4.8	4.2	3.8	3.4	3.1
80–89	1.48	1.32	61.8	15.8	11.3	08.8	7.2	6.1	5.3	4.7	4.2	3.8	3.4
90–99	1.54	1.44	66.3	17.3	12.3	09.6	7.9	6.6	5.8	5.1	4.5	4.1	3.8
100–109	1.60	1.55	70.5	18.6	13.3	10.3	8.5	7.2	6.2	5.5	4.9	4.4	4.0

on. Minute volume was then increased until the circuit pressure was 20 cmH_2O (peak). The decrease in resting height of the bellows in one minute represented the actual leak during controlled ventilation. A leak of less than 25 ml/minute was accepted.

The total circuit volume was measured by flushing the circuit with oxygen until the oxygen analyser read 100%. The test lung fitting to the patient port was emptied and the ventilator bellows were filled to the 1200 ml spirometer mark. One litre of N_2O was then delivered to the closed circuit; measured by the rising of the ventilator bellows to the 200 ml spirometer mark. The O_2 and N_2O were mixed by turning the ventilator on for one minute. The circuit volume was simply calculated from the fall in O_2 concentration. The circuit volume was 6.9 litres including the working volume of the bellows.

The circuit compliance was measured by squeezing the reservoir bag to pressurize the system to 20 cmH_2O. The manual bag selector was then switched to ventilator position. The resultant displacement of the ventilator bellows height while the reservoir bag was squeezed, was a measure of the circuit compliance at 20 cmH_2O. The circuit compliance was 10 ml/cmH_2O.

Liquid isoflurane was injected into the expiratory limb of the circuit using the Ivac-700 syringe pump. The sealing between the polyethylene tube of the injection set and the plastic distal locking Luer fitting was noticed to dissolve in isoflurane. It was eliminated and the cut end of the tube was fitted with an 18-gauge needle. The needle was inserted through the thick wall rubber connexion between the expiratory limb and the main block of the circuit. The heat of expiration together with distance and volume of gas between the injection port and the patient ensured isoflurane evaporation. The injection site was kept at a lower level than the tracheal tube to prevent accidental drainage of any liquid isoflurane collection into the patient. Twenty-five ml isoflurane were aspirated into the 50 ml syringe of the pump. The injection tube set (2 ml capacity) was also filled up to the needle with isoflurane. The pump was then set to the injection rate used during the first 4 minutes, and kept in the standby mode before induction of anaesthesia.

Patients and anaesthetic technique. The technique was used in 26 adult (ASA grade 1 and 2) patients undergoing middle ear surgery (tympanoplasty and mastoidectomy), 14 males and 12 females, between 15 and 53 years, weight between 37 and 109 kg (Table 2). The local scientific ethics committee approved the study and informed consent was obtained from each patinet.

Each patient received diazepam 0.2 mg/kg by mouth 2 hours before the operation. Intravenous fentanyl 1 μg/kg was given before induction. Thiopentone 5 mg/kg was followed by pancuronium 0.1 mg/kg. The lungs were ventilated using a facemask and high oxygen flow for 2 minutes; there was sufficient time to raise the oxygen concentration above 60% in the circuit. The vocal cords were sprayed with lignocaine and the trachea was intubated with a cuffed tube before the patient was connected to the circuit. Ventilation was controlled at a rate of 10/minute. Tidal volume was set according to body weight using the Ohio Ventilation Calculator after correction for circuit compliance. Oxygen fresh flow was manipulated to maintain constant circuit volume. Isoflurane injection was then started (zero time), at a rate according to the proper weight

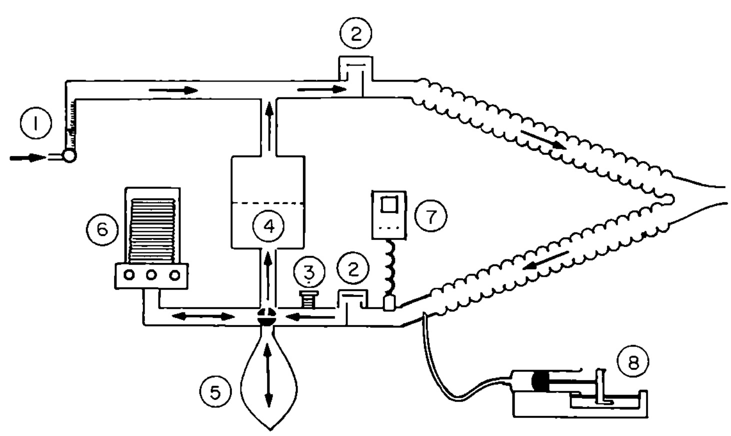

Fig. 1. Scheme of circuit arrangement. 1, Oxygen flow meter; 2, unidirectional valves; 3, pop-off valve; 4 soda-lime canister; 5, reservoir bag; 6, rising bellows ventilator; 7, oxygen analyser; 8, syringe pump.

Table 2. Patients and anaesthetic details.

	Age (years)	Weight (kg)	Operation time (minutes)	Isoflurane injection (minutes)	Coasting time (minutes)	Recovery time (minutes)	Oxygen flow (ml/minute)	Liquid inoflurane used (ml)
Range	15–53	37–109	40–175	30–160	4–20	5–25	200–325	6–16
Mean	28.5	65.6	82.3	73.3	8.9	10.5	232.3	10.3
SD	08.6	15.7	32.6	31.9	4.4	06.7	040.5	02.6

group (Table 1) and the injection rate was changed at the end of each time interval. Arterial blood pressure was monitored oscillometrically using Dinamap (Critikon 1846 SX), and ECG was monitored using standard lead II (Medishield Monitor M1). The rate of isoflurane injection was adjusted for the lower or higher weight group, appropriate to the time interval, if the mean arterial blood pressure (MABP) became less than 60 mmHg or more than 90 mmHg. In addition, a second dose of fentanyl 1 μg/kg was given whenever the heart rate increased above 100/minute. Before starting surgery, 10 ml lignocaine 1% in 1/200 000 adrenaline were infiltrated in the surgical field, and the patient was tilted 5° head up. Towards the end of the operation, the isoflurane injection was stopped, while the circuit was maintained closed. This coasting period was kept as often as possible equal to the square root of isoflurane injection time.

At the end of the operation, the circuit was opened and replaced by a Magill's attachment, using high oxygen flow to enhance recovery, and residual neuromuscular blockade was antagonised with neostigmine and atropine before tracheal extubation. An arterial blood sample was obtained before opening the circuit at the end of the operation for blood gas measurement, using the self-calibrating Instrumentation Laboratory System 1303 blood gas analyser after correction to nasopharyngeal temperature. Serum catecholamine concentrations were measured in three patients before induction of anaesthesia and before opening the circuit near the end of the operation by radioenzymatic assay based on the method described by Peuler and Johnson 1977.[8] The duration of operation, isoflurane injection, coasting and recovery were recorded. Recovery duration was from the time the circuit was opened at the end of the operation until the patient responded to verbal commands.

A paired t-test was used to test for statistical significance between variables. Regression analysis was performed between some variables, and parameters of the regression equation were calculated using the Microstat statistical package.

Results

In 26 patients a mean (SD) of 10.3 (2.6) ml liquid isoflurane were injected in a totally closed circuit over 73.3 (31.9) minutes, for operations lasting 82.3 (32.6) minutes. When the isoflurane injection was stopped there was a coasting period of 8.9 (4.4) minutes (Table 2). The mean recovery time was 10.5 (6.7) minutes.

The mean fresh oxygen flow to maintain constant circuit volume was 232.3 (40.5) ml/minute. It showed a good correlation with patient body weight ($r = 0.7312$). The regression equation was O_2 ml/minute $= 109.2 + (1.88$ weight). Although tracheal intubation was followed by a significant increase in MABP, isoflurane injection induced a steady significant decrease that was maintained throughout the operation at a level about 75% of that before induction, and was readily reversed to normal during recovery (Table 3). In two patients the MABP reduced below 60 mmHg, while in three patients it increased above 90 mmHg, but they all responded well to changing the rate of isoflurane injection one step in the appropriate direction; Table 4 showes the time, duration, direction and magnitude of deviation from predicted rates of isoflurane delivery in

Table 4. Time, duration, direction and magnitude of deviation from planned rates of isoflurane injection in 5/26 patients.

Serial	Start time*	Duration (minutes)	Direction and magnitude (steps)†
1	12	8	−(1)
2	42	8‡	−(1)
3	15	24‡	+(1)
4	15	49‡	+(1)
5	30	6	+(1)

*minutes from starting isoflurane injection.
†+/− = higher or lower weight group injection rate.
‡until the end of isoflurane injection.

Table 3. Pulse rate and MABP before, during and after isoflurane injection.

Time (minutes)	Before induction	Zero time	5	10	15	30	45	60	90	120	Recovery
$n =$	26	26	26	26	26	26	23	20	11	4	26
Pulse rate (/minute)											
Range	55–138	60–150	80–144	80–141	75–133	75–136	72–119	70–110	68–105	68–82	60–119
Mean	93.2	117.9**	109.9**	109.9**	107.2**	100*	93.8	88.9	84.8*	75	90.3
(SD)	(21.0)	(021.2)	(016.2)	(17.8)	(017.1)	(016.5)	(13.8)	(19.2)	(13.6)	(5.7)	(17.3)
MABP (mmHg)											
Range	80–121	88–165	63–104	61–92	55–95	60–98	58–95	59–93	60–92	68–98	85–128
Mean	96.0	115.8**	87.8*	75.8**	72.2**	73.7**	73.2**	71.6**	72.9**	80	102.2*
(SD)	(09.8)	(017.3)	(09.3)	(10.2)	(09.6)	(11.4)	(09.2)	(09.7)	(10.5)	(13.4)	(013.9)

*$p < 0.05$ compared to before-induction value.
**$p < 0.001$ compared to before-induction value.

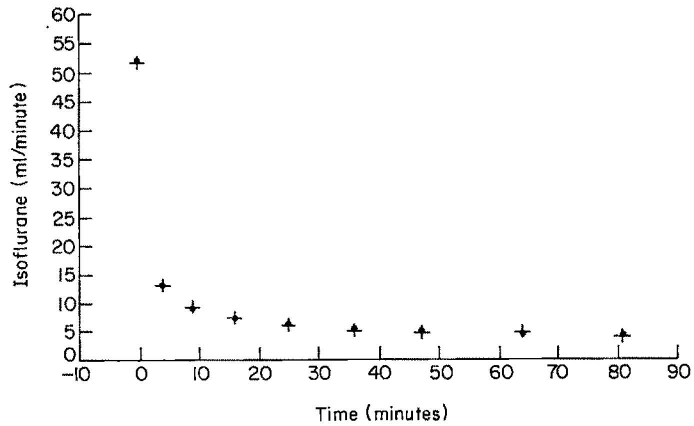

Fig. 2. Predicted versus delivered mean isoflurane injection rates (●, predicted; +, delivered).

the five patients. Figure 2 shows the mean predicted and delivered (modified) injection rates; the Chi-squared goodness of fit test showed no significant difference between the two rates (Chi-squared = 0.1144). Intra-operative surgical conditions were described as excellent by the surgeon. Mean pulse rates were maintained significantly higher than that before induction for more than 30 minutes (Table 3). Twelve patients needed an additional dose of fentanyl to control tachycardia. None of the patients developed arrhythmias.

Before opening the ciruit, mean F_{EO_2} was 0.78 (0.09) and mean arterial blood gas values were within the normal range (Table 5). Plasma adrenalin (PA) showed some decrease while plasma noradrenaline (PNA) showed some increase relative to the pre-induction value, but all were within the normal range (Table 6).

Discussion

Most of the patients responded well to the planned isoflurane injection rates (Table 1). Variations in response encountered in some patients were expected. Westenskow estimated 28% anaesthetic requirement variability between patients.[9] Syringe pump delivery of liquid isoflurane maintained steady anaesthesia and avoided the reported fluctuations that result from bolus injection of the unit dose. Ernst[10] suggested reducing or even omitting the fourth unit dose at the 9th minute as the myocardium is well saturated by this time. Continuous delivery of the unit dose by syringe pump over the 7 minutes of the third time interval should be much safer than its bolus injection. Close observation and vigilance are still required but do not detract from the technique. The injection rates table saved many calculations, and changes of injection rate to that for the higher or lower weight group were as easy and effective as changing a vaporizer setting for a smooth correction of the anaesthetic response.

Isoflurane has been shown to induce easily controlled and reversible hypotension by peripheral vasodilatation, with little effect on pulmonary gas exchange,[11] cardiac output and rhythm[12] in neurosurgical patients. Macnab *et al.*[13] used 2–4% isoflurane-inspired concentrations to attain and maintain MABP of 50 mmHg. Newman *et al.*[14] found that global cerebral O_2 supply–demand balance was favourably influenced during isoflurane-induced hypotension.

Isoflurane tends to increase heart rate, as has been observed in this study. It could be explained by stimulation of the uninhibited baroreceptor reflex by induced hypotension.[1] As the increase in heart rate is dose related and more evident in younger adults, potentiated by pancuronium when nitrous oxide was not used,[15] higher doses of fentanyl might have been used.

Table 5. Arterial blood gases at the end of the operation (n = 26).

	F_{EO_2}	PH	Pa_{CO_2} mmHg	Pa_{O_2} mmHg	Base excess
Range	0.6–0.92	7.26–7.45	26–41	211–480	−8–+5
Mean	0.78	7.37	32.7	352.9	−3.0
± SD	0.09	0.048	4.4	80.8	2.7

Table 6. Plasma catecholamine levels (range and (mean), n = 3).

Normal value	Plasma adrenaline concentration (up to 125 ng/litre)	Plasma noradrenaline concentration (up to 450 ng/litre)
Before induction	74–119 (93)	103–231 (153.3)
Before opening the circuit	55–105 (86.3)	122–318 (205.3)

The patient's oxygen consumption equated to the oxygen flow rate, and showed good correlation with patient body weight; its mean value is in reasonable agreement with previous observations.[16,17] The blood gas data showed no evidence of metabolic changes or inadequate tissue perfusion. The mean FEO_2 of 0.78 recorded before opening the circuit can be reduced by shortening the initial denitrogenation process to the desired FEO_2. The amount of nitrogen dissolved in tissues of an average adult is only one litre,[18] and the rate of nitrogen accumulation in a closed circuit is much less than 10% after 2 hours.[19] An FEO_2 of 0.4–0.5 might be a reasonable O_2 fraction at which to start closing the circuit.

The minimal changes in catecholamine levels that have been recorded in three of this study's patients suggest attenuation of catecholamine response by isoflurane. Macnab *et al.* 1988[13] used higher doses of isoflurane and fentanyl to induce hypotension. They recorded a significant fall in plasma adrenaline during hypotension, while plasma noradrenaline remained unchanged and plasma renin activity rose, indicating an attenuated stress response to induced hypotension.

Using the coasting technique, followed by a non-rebreathing system at the end of the operation to bring inspired anaesthetic concentration to zero, patients recovered after 10.5 (6.7) minutes. During the coasting period, blood and brain concentrations decreased slowly because of the uptake of isoflurane by muscle and fat. Opening the circuit and the use of a non-rebreathing system add and enhance elimination through the lungs. Charcoal filters were used by other workers for the same purpose while maintaining the circuit closed.[20,21] The coasting period can last about two times the square root of elapsed time before alveolar concentration reaches 1 MAC.[6] Shorter coasting periods were used in this work to prevent early coughing or movement before the end of the operation.

During this study a mean of 10.3 ml liquid isoflurane was injected in the closed circuit to maintain anaesthesia for a mean of 82.3 minutes. If a non-rebreathing system with 6 litres fresh O_2 flow was used, more than 40 ml liquid isoflurane would have been used to maintain the same level of anaesthesia. As isoflurane is more than 10 times as expensive by volume than halothane, a 300% saving should be considered. The cost of refilling the absorbers with soda lime would be minimal compared to the saving on the cost of isoflurane. Ernst and Pearson[22] found a 470% saving in costs of isoflurane when used in a closed circuit during 180-minute operations. This method would be more economical in longer operations. As newer, more expensive agents, such as desflurane, become available, such techniques will be of even greater importance.

Monitoring inspired and end-tidal gases and anaesthetics will need to be widely undertaken to conform to the recent guidelines on the standards of monitoring.[23] This should increase the feasibility and safety of practising closed circuit anaesthesia, and the potential also exists for recouping the cost of these expensive monitors.

Using standard equipment available in most modern operating theatres, the described technique for closed-circuit isoflurane injection has been proved safe, economic, and adaptable to patient variability as regards uptake and response to isoflurane. The implemented injection rate table saved many calculations, guided redosing and served as a record.

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Antireflux valves in intravenous opioid analgesia: are they necessary?

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Summary

A study was conducted in patients receiving intravenous opioid analgesia to determine the incidence and degree of retrograde flow along the parallel gravity-driven infusion line. From 1187 hours of observations retrograde flow was found in 2.5% of the total time. In 70% of these cases this was equivalent to less than 1 mg of pethidine and in 96% this was equivalent to less than 5 mg of pethidine. The need for routine use of antireflux valves during intravenous opioid analgesia is therefore questioned.

Key words

Equipment; infusion systems.
Analgesics; morphine, pethidine, papaveretum.
Analgesic techniques; infusion, continuous.

Intravenous opioid infusions are becoming increasingly popular for postoperative analgesia. Recently it has been suggested that one-way valves should be used with all opioid infusions to prevent the theoretical possibility of retrograde flow of the infusion along a parallel gravity-driven infusion line.[1] This volume could subsequently be infused as a bolus once the blockage of the intravenous cannula or vein was cleared. To date there have been no studies to show whether this possibility occurs in clinical practice or to what extent.

This trial was conducted to determine the frequency and extent of episodes of retrograde flow and to assess the clinical significance of the possible bolus administration of that volume of opioid infusion.

Methods

For a 4 month period all patients receiving an intravenous opioid infusion for postoperative analgesia had 1 ml (10 mg) of methylene blue added to the opioid solution. This infusion consisted of 500 mg pethidine, 100 mg papaveretum or 50 mg morphine in 500 ml of physiological saline. The resulting solution became a clearly visible blue colour. The opioid solution was usually infused at rates of 10 to 40 ml/hour through a Travenol (Flo-gard 8000) volumetric infusion pump. It is standard procedure at Sir Charles Gairdner Hospital for patients receiving such infusions to have hourly observations of pulse, blood pressure and respiratory rate. During the course of the study, in addition to these observations, the nursing staff noted the presence, if any, of retrograde flow of the opioid infusion along the parallel intravenous line and noted its distance. The retrograde flow was measured in centimetres from the point of joining of the two infusions. These observations were continued until the initial bag of opioid infusion was discontinued or completed.

Results

Adequate documentation was obtained from 82 patients, totalling 1187 hours of postoperative observations (mean 14.5 hours per patient). There were 30 episodes of retrograde flow (2.5% of total observation time), two of which were described as 'minimal'; no exact distance was recorded and so these episodes were not included in the subsequent calculations.

Figure 1 shows the frequency distribution of the episodes of retrograde flow measured in centimetres. There were 17 episodes of less than 10 cm, five episodes between 10 to 20 cm, two between 30 to 40 cm and four greater than 40 cm.

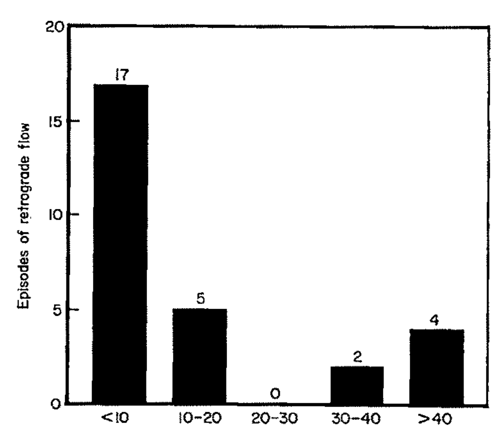

Fig. 1. Frequency distribution of episodes of retrograde flow measured in cm.

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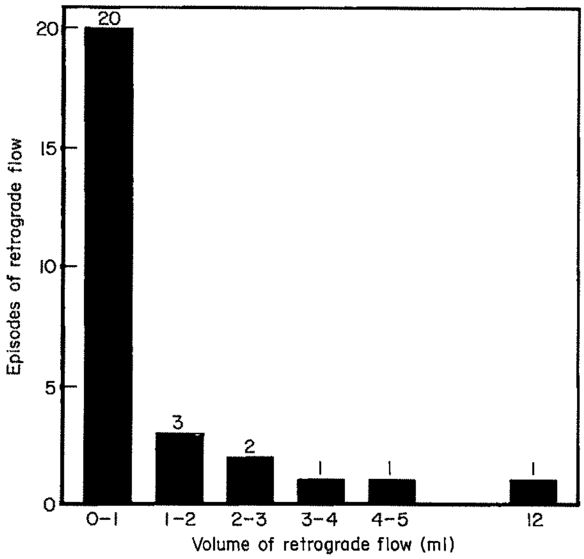

Fig. 2. Frequency distribution of episodes of retrograde flow by volume.

TUTA giving sets were used, the internal diameter of which are such that 1 cm of retrograde flow contains a volume of 0.0625 ml. Figure 2 shows the frequency distribution of the episodes of retrograde flow by volume. Seventy per cent of the retrograde flow was less than 1 ml and 96% was less than 5 ml. This is equivalent to 1 mg and 5 mg of pethidine respectively. The largest volume of retrograde flow was 192 cm, representing 12 mg of pethidine.

Discussion

The greater frequency of use of intravenous opioid infusions has highlighted the increased cost of one-way valves in the parallel hydration line. These are Aus $5.00 compared to normal intravenous giving sets at Aus $1.75. This has occurred without clinical studies to show that retrograde flow of the opioid infusion is a significant problem.

In the present study, there was no retrograde flow during 97.5% of the total period of observation. When retrograde flow occurred, 70% was less than 1 ml and 96% less than 5 ml. These volumes are likely to be less than the hourly infusion rate of the opioid, and, as such, if administered as a bolus, would have minimal deleterious effects. Moreover, this retrograde flow volume is the amount of drug the patient was due to receive in the preceding hour but failed to. The use of high concentration opioid infusions at low infusion rates would not change the significance of these findings as the lower infusion rate would cause a proportionally lower volume, and therefore dose, to flow in a retrograde direction.

In conclusion, we have shown over a large number of hours of observation, that retrograde flow occurs rarely and it is almost always of minimal volume. Therefore, the use of one-way valves may be an unnecessary additional expense to an already overburdened hospital budget.

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Oral fluids prior to day surgery

The effect of shortening the pre-operative fluid fast on postoperative morbidity

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Summary

One hundred day surgical patients undergoing first trimester termination of pregnancy were randomly allocated to receive either 150 ml of clear fluid 1.5–2 hours before anaesthesia or to remain fasted from midnight the night before. Patients were anaesthetised using a total intravenous technique which consisted of propofol and alfentanil. No adverse intra-operative events were noted in either group. There were no significant differences in immediate recovery time, or pain, nausea and headache scores at 30 or 120 minutes following recovery. The fasted group had less pain ($p < 0.05$) at 60 minutes after recovery than the fluid group, although the mean pain scores in both groups were low. Eighty two per cent of the patients returned questionnaires about pain, nausea and headache scores on arriving home, and at 12 and 24 hours after surgery. There were no significant differences between the two groups. In conclusion, pain, nausea and headache scores are low following total intravenous anaesthesia with propofol and alfentanil for termination of pregnancy and these were unaffected by the administration of 150 ml of clear fluid given approximately 1.5 hours pre-operatively.

Key words

Fluid balance; oral fluids.
Anaesthesia; outpatient.
Anaesthetics, intravenous; propofol, alfentanil.

At induction of anaesthesia gastric contents may consist of saliva, gastric secretions and ingested material remaining within the stomach. Fasting patients continue to produce saliva and up to 50 ml/hour of gastric secretions.[1] However, the stomach is a dynamic organ and neither ingested fluid, which passes rapidly through the pylorus, nor secretions accumulate in healthy individuals. Conversely, food passes through the stomach at variable rates, sometimes taking up to 12 hours.[2,3] In contrast, water has a 50% emptying time of only 12 minutes.[4] Clear fluids have a rapid gastric emptying rate because they offer minimal resistance at the pylorus and because they increase gastric emptying.[5] Recently, traditional pre-operative fasting practices have been questioned since they cause hunger, thirst and dehydration.[6,7] Prolonged fasting may only be justified if it consistently minimizes the volume of gastric contents which could be regurgitated or vomited during anaesthesia. Studies have demonstrated that healthy patients who drink clear fluids 2–4 hours pre-operatively do not have larger gastric fluid volumes than those who fast from midnight or longer.[8–13]

At least one North American teaching hospital has altered its fasting guidelines for day surgical patients, from nil by mouth after midnight, to giving 150 ml of oral fluid 3 hours before surgery. Since the adoption of these guidelines in day case surgery, it has been shown that the reduction of the fluid fast to 3 hours neither increased nor decreased the risk of regurgitation or aspiration pneumonitis.[14] Other workers have reported that drinking 150 ml of water 2 hours before induction of anaesthesia changed neither residual stomach volume nor pH.[15]

The aim of the present study was to assess the effect of reducing the pre-operative fluid fast on postoperative morbidity, with specific reference to nausea, vomiting and headache.

Methods

The study had District Ethics Committee approval. One hundred adult females, ASA grade 1 or 2 who had given written informed consent, were entered into this prospective randomised, double-blind, parallel group study. All were scheduled for first trimester termination of pregnancy in the Day Surgery Unit.

Patients included in the series had an age range of 15–40 years and a weight range of 40–95 kg. Those with a known history of gastrointestinal disease, migraine or cluster headaches and who required premedication were not studied. Patients were randomly allocated by the nursing staff to one of two groups. Group A (the control group) were given nil by mouth from midnight. Study group B were given 150 ml of clear fluid, either water or an orange drink. This was given 2 hours before general anaesthesia. Neither the anaesthetist nor the observer knew whether or not fluids had been administered.

Thirst and hunger were assessed using 100 mm linear analogue scales after recruitment to the study and immediately before induction of anaesthesia. This also served to introduce the patients to the concept of the linear analogue score.

Both groups received the same general anaesthetic technique administered by a consultant anaesthetist (T.W.O.).

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Table 1. Mean (SD) values for age, weight, parity, fluid fast time and type of pre-operative drink.

	Fluids group	Fasted group
n	50	49
Age; years	26.3 (7.0)	25.8 (7.0)
Weight; kg	59.9 (8.4)	62.4 (9.6)
Parity: Primiparous	21 (42%)	25 (51%)
Multiparous	29 (58%)	24 (49%)
Last drink to induction interval; minutes	92.3	734
Drink type: Water	12 (24%)	
Orange	38 (76%)	

Induction was with alfentanil 3 μg/kg and propofol 2.5 mg/kg. Anaesthesia was maintained with a propofol infusion of 9 mg/kg/hour using an Ohmeda 9000 syringe driver. A further bolus of alfentanil was given before dilatation of the cervix. The patients breathed oxygen-enriched air via a parallel Lack circuit. Pulse, indirect blood pressure, electrocardiogram (ECG), and oxygen saturation were monitored throughout. Syntometrine was administered only on the request of the gynaecologist, whose status was at least that of a registrar holding the MRCOG.

The immediate recovery time, i.e. the time from cessation of the propofol infusion to awakening was recorded with the Steward score.[16] After the patient awoke, pain, nausea and headache were assessed at 30, 60 and 120 minutes using linear analogue scores.

At the end of this 2-hour period, patients were discharged from the day surgery unit. They were given a stamped, addressed envelope and a questionnaire which included three further pain, nausea and headache scores to be completed when they arrived home, and 12 and 24 hours following their operation.

Results were analysed using the two-tailed *t*-test or Chi-squared tests and Wilcoxon Signed rank sum tests as appropriate.

Results

Although 100 patients were studied, one, who was randomised to the starved group, was withdrawn because she vomited before the induction of anaesthesia.

Table 1 shows the mean (SD) values for age, weight, parity, fluid-fast time and type of pre-operative fluids given in the series. There were no significant differences between the groups.

Table 2 shows the mean (SD) doses of propofol and alfentanil administered. Duration of surgery and anaesthesia are also shown. Both groups were similar in these respects.

Table 2. Mean (SD) values for doses of propofol and alfentanil, anaesthesia time, surgery time and immediate recovery time.

	Fluids group	Fasted group
Propofol; mg		
Induction	157.2 (19.1)	159.6 (18.6)
Maintenance	88.7 (41.9)	98.9 (41.9)
Total	247.1 (45.8)	258.7 (51.1)
Alfentanil; μg	478.0 (106.5)	495.8 (61.7)
Immediate recovery time; minutes	6.8 (2.1)	6.8 (1.7)
Duration; minutes		
Anaesthesia	6.9 (1.9)	7.0 (2.2)
Surgery	5.1 (1.9)	5.2 (2.1)

Table 3. Median (range) visual analogue scores for pre-operative hunger and thirst, questionnaire response rate and syntometrine administration.

	Fluids group	Fasted group
Thirst scores; mm		
on admission	51 (1–90)	51 (5–100)
immediately before operation	29 (0–91)***	66.5 (6–100)***
Hunger scores; mm		
on admission	26 (0–100)	19.5 (1–100)
immediately before operation	40 (0–100)**	32.5 (1–100)**
Questionnaire response		
Yes	42 (84%)	39 (79.6%)
No	8 (16%)	10 (20.4%)
Syntometrine given?		
Yes	3 (6%)	8 (16.4%)
No	47 (94%)	41 (83.7%)

**$p < 0.01$ (within-group comparison).
***$p < 0.001$ (within and between groups comparison).

Table 3 shows the median (range) values for visual analogue scores for pre-operative hunger and thirst. Immediately before general anaesthesia the thirst score showed a significant difference ($p < 0.001$) between the fluid and the fasted group, and within each group there was also a significant difference in thirst scores on admission and before anaesthesia. The hunger score showed a significant increase ($p < 0.01$) in both the fluid and fasted groups between admission and induction of anaesthesia.

Table 4 records the median (range) visual analogue scores for pain, nausea and headache during the first 24 postoperative hours. The sole significant result was for pain at 60 minutes. The fasted group had a significantly lower pain score ($p < 0.05$) than the fluid group. Low scores for all three parameters were recorded for both treatment groups throughout the postoperative period.

Table 4. Median (range) visual analogue scores for pain, nausea and headache during the first 24 postoperative hours.

	Fluids group	Fasted group
Pain scores; mm		
30 minutes	33 (1–85)	40 (0–93)
60 minutes	25 (1–90)	14 (1–77)*
120 minutes	13 (1–91)	5.5 (0–59)
At home	10 (0–80)	8 (0–77)
12 hours	4.5 (0–43)	3 (0–75)
24 hours	1 (0–28)	1 (0–73)
Nausea scores; mm		
30 minutes	2.5 (0–90)	1 (0–68)
60 minutes	1 (0–90)	1 (0–45)
120 minutes	1 (0–40)	1 (0–60)
At home	1 (0–40)	1 (0–16)
12 hours	1 (0–20)	1 (0–45)
24 hours	1 (0–25)	1 (0–26)
Headache scores; mm		
30 minutes	1 (0–29)	1 (0–67)
60 minutes	1 (0–70)	1 (0–63)
120 minutes	1 (0–16)	1 (0–28)
At home	1 (0–18)	1 (0–51)
12 hours	1 (0–16)	1 (0–50)
24 hours	1 (0–20)	1 (0–11)

*$p < 0.05$ (between group comparison).

Discussion

Pre-operative fasting has been a controversial subject since investigators demonstrated that healthy patients given clear fluids 2–4 hours pre-operatively do not have larger gastric fluid volumes than those who fast from midnight.[8-13] Clear fluids do not appear to increase the incidence of regurgitation or vomiting during anaesthesia; certainly this was the experience in this present study. Pre-operative thirst and hunger are an unrecognised source of morbidity and they may contribute to postoperative nausea and vomiting.

This study has shown that there was a significant decrease in thirst in the group given fluids before surgery; however, this group also experienced a significant increase in hunger. This has previously been shown in premedicated, but not in unpremedicated, patients.[17] It has also been reported that a reduction in thirst may improve perioperative behaviour in children.[18]

One patient in the starved group, vomited just before induction of anaesthesia and was withdrawn from the series. No member of the fluid group vomited or regurgitated during anaesthesia, which lends support to the use of pre-operative fluids in day case surgery.

Postoperatively the fasted group had a significantly lower pain score at 60 minutes ($p < 0.05$). However, all pain scores were low and the clinical significance of this result could be questioned.

Postoperative nausea and headache scores were low and there were no significant differences between the two groups. Other workers have previously commented on the low incidence of nausea and vomiting when pre-operative fluids are given; however, they made no comparison of the incidence of these side effects between fasted and unfasted patients.[17]

The results of this study suggest that there is no effect on postoperative morbidity if patients are given clear fluids 2 hours before operation and confirms a reduction in pre-operative thirst following the use of clear fluids. Patients in this series did not vomit or regurgitate following an oral fluid challenge before anaesthesia. The incidence of vomiting in this study was 1%, significantly lower than previously reported in outpatient gynaecological surgery.[19] The general anaesthetic combination administered, propofol and alfentanil, is known to cause a marked reduction in postoperative nausea and vomiting.[20,21] Mean linear analogue scores for nausea were low. We were unable to compare our study with previous studies that quote percentage nausea rates, without a quantitative measure of nausea being taken into account.

In conclusion, we have shown that clear fluids may be safely given 2 hours pre-operatively to adult patients undergoing day case surgery without any risk of intra-operative aspiration or increase in postoperative morbidity. Further studies should now be undertaken to investigate the effect of pre-operative fluid administration on children awaiting surgery.

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Effect of prior administration of cold saline on pain during propofol injection

A comparison with cold propofol and propofol with lignocaine

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Summary

A single-blind, randomised, controlled study was undertaken to compare the efficacy of three methods of preventing pain during injection of propofol on induction of anaesthesia. Patients were allocated randomly to receive unmodified propofol, propofol with 0.05% lignocaine, propofol at 4°C and unmodified propofol preceded by 10 ml of 0.9% saline at 4°C. Prior injection of cold saline reduced the incidence of pain and discomfort significantly (22%) compared with unmodified propofol (75%; $p < 0.005$) and was similar to that after cold propofol (33%) and propofol with lignocaine (44%). There was no significant difference between the treatment groups.

Key words

Anaesthetics, intravenous; propofol.
Pain.

The incidence of pain on intravenous injection of propofol during induction of anaesthesia has been found to vary between 30 and 90%.[1,2] Mixing propofol with lignocaine or administering propofol at 4°C reduces the incidence of pain.[3–6] The mechanism of action of these techniques is not clear, although Scott *et al.* have suggested an effect on enzymatic cascade.[7]

Previous work has shown that 0.9% saline at room temperature is ineffective at preventing pain.[5] The aim of this study was to assess the effectiveness of pretreatment of the vein on the dorsum of the hand with 0.9% saline at 4°C.

Method

One hundred and nine patients (ASA 1–2; 50 male) aged 19–80 years presenting for elective surgery were recruited. Local ethics committee approval and informed patient consent was obtained.

Temazepam 10–20 mg was given 1 hour before surgery. On arrival in the anaesthetic room, a 23-gauge cannula (Venflon) was inserted into the largest visible vein on the dorsum of the nondominant hand and patients were allocated randomly to one of four groups. Group P received unmodified propofol, group PL propofol mixed with lignocaine to a concentration of 0.05%, group CP propofol at 4°C, group CS propofol immediately preceded by 0.9% saline 10 ml at 4°C injected over 15 seconds. All patients were then given propofol 2.5 mg/kg in an identical fashion. Propofol 50 mg was administered over 5 seconds and pain was assessed after 5 seconds during which propofol was not given. Propofol administration was then resumed and after 50% of the calculated dose had been given a second pain score was obtained. Finally, the rest of the induction dose was administered.

Pain was assessed by asking the patient to describe any sensation in the arm or hand as 'no discomfort', 'uncomfortable', 'painful' or 'very painful'. No objective assessment was added by the anaesthetist. The worst pain of the two scores obtained for each patient were analysed.

Data were compared using one-way analysis of variance and the Chi-squared test with Yates' correction as appropriate.

Results

There were no differences between the groups with respect to age, weight, sex, and induction dose of propofol (Table 1). The distribution of pain scores in each group are shown in Fig. 1. After pretreatment with saline at 4°C, 21 patients (78%) felt no discomfort or pain during subsequent injection of propofol, compared with 15 (56%) in the lignocaine group, 18 (67%) in the cold propofol group and seven (25%) in the unmodified propofol group. The pain scores were significantly lower in all treatment groups when compared with unmodified propofol; pretreatment with 0.9% saline at 4°C had the lowest pain scores, although these were not significantly lower than the other treatment groups.

Discussion

The incidence of pain on injection of unmodified propofol in the present study was similar to others.[3,4] The addition of lignocaine, propofol at 4°C and preceding unmodified propofol with 0.9% saline at 4°C reduced the incidence of pain significantly. There was no significant difference between these treatment groups.

Several authors have found that lignocaine in propofol reduced the pain on injection,[5,8] and McCrirrick and

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Table 1. Patient characteristics, mean (SEM). There were no significant differences between the groups.

Group	Unmodified propofol	Prior saline at 4°C	Propofol and lignocaine	Propofol at 4°C
n	28	27	27	27
M/F	14/14	12/15	14/13	10/17
Age; years	41.7 (2.6)	41.9 (2.95)	47.7 (2.7)	46.6 (3.3)
Weight; kg	69.2 (1.9)	66.8 (1.8)	69.2 (2.0)	68.2 (1.3)
Dose; mg	175.0 (6.8)	158.1 (6.8)	162.6 (5.9)	161.5 (6.8)

Hunter showed that propofol injected at 4°C had a similar effect.[6] We have confirmed these findings. The analgesic effect of lignocaine may occur because of a local anaesthetic effect or an inhibitory effect on the enzymatic cascade which leads to release of kinins.[7] Similarly, cold propofol may have a local anaesthetic effect on the vein wall or reduce the speed of the enzymatic cascade around the injected propofol. In the present study it is unlikely that prior injection of cold saline would have any significant effect on the temperature of blood during the subsequent injection of propofol at room temperature. A local anaesthetic effect on the vein wall is a more likely explanation, but this is only speculative.

In conclusion, pretreatment with 0.9% saline at 4°C provides a safe and simple method of reducing the pain on injection of propofol without the addition of local anaesthetic agents or the need for refrigeration of propofol.

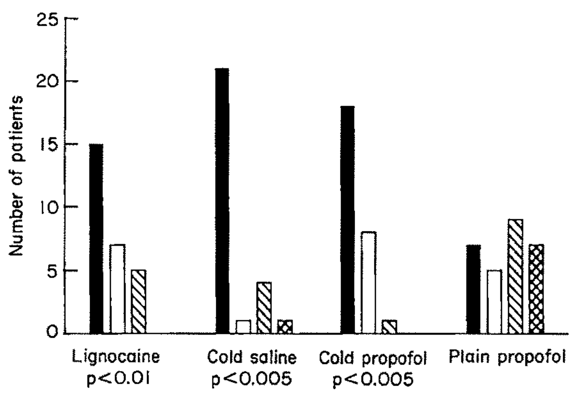

Fig. 1. Pain scores for patients in each group during injection of propofol. Significance compared with unmodified propofol. There were no significant differences between treatment groups. ■, no discomfort; □, uncomfortable; ▧, painful; ▩, very painful.

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Policies for oral intake during labour

A survey of maternity units in England and Wales

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Summary

A postal survey was conducted to gain information on the use of policies on oral intake, selection of mothers and type of intake given during established labour by all maternity units in England and Wales. A response rate of 91.6% (351 out of 383) was achieved; 79.5% of units had a written policy for oral intake, 96.4% of units allowed mothers some form of oral intake and 68.3% of these units selected mothers according to risk categories. Of the 268 units allowing oral intake, 67.2% gave drink only and 32.8% drink and food. Of those allowing food, all but 13.6% had a selection policy. Of the 85 units not selecting mothers, 78.8% gave water only; the remaining 21.2% gave water and other drink or food. This survey demonstrates a wide variation in policies for oral intake during labour.

Key words

Anaesthesia; obstetric.
Complications; inhalation of gastric contents.
Labour; oral intake.

Aspiration of gastric contents is a significant cause of maternal mortality associated with obstetric anaesthesia.[1] Death may result from asphyxiation caused by large food particles or pneumonitis due to aspiration of acid or small food particles.[2–4] The methods of reducing the risk to the pregnant mother include: the restriction of oral intake during labour, the neutralisation of gastric contents by antacids and the use of H_2-receptor antagonists.[5] Previous studies of gastric emptying in pregnancy and labour have produced conflicting results,[6,7] and feeding policies during labour are not universally agreed.

The aims of this survey were to establish: the extent of use of policies for oral intake during established labour in maternity units in England and Wales, the criteria used for selection of mothers who would receive drink or food and the types of drink or food allowed.

Methods

A mailing list of maternity units in England and Wales was prepared using addresses supplied by the Royal College of Obstetricians and Gynaecologists, verified and supplemented by reference to the 1988 NHS Yearbook. The 383 units on this list were each sent a questionnaire, a stamped, self-addressed envelope and a covering letter addressed to the Labour Ward Nursing Officer. A reminder with similar contents was sent 6 weeks later and a total of 3 months was allowed for the return of the questionnaires. The survey was conducted between June and September 1989. The questionnaire asked six main questions as shown in Table 1. The questions were answered by ticking boxes and space was provided for additional information suggested in the questions.

Results

Of the 383 questionnaires sent, 351 were returned, representing a reply rate of 91.6%. Seventy-three replies were from units that no longer had a labour ward and therefore were excluded from further analysis. There was no policy for oral intake during labour in 20.5% of units. The majority (96.4%) allowed oral intake and of these 68.3% selected mothers for type of food or drink (Table 2).

The selection of mothers for oral intake based on degree of obstetric risk showed wide variation (Table 3). Of the 268 units allowing oral intake during labour 180 gave drink only and 88 drink and food. Of those allowing food, all but 12 had a selection policy. Of the 85 units not selecting mothers for type of oral intake, 67 gave water only, six water and other drink and 12 drink and food. The 12 units allowing food but not selecting mothers were small units accepting uncomplicated primigravid and multigravid patients.

The choices of drink and food are shown in Table 4.

Discussion

This survey demonstrated a wide variation in policy for oral intake during established labour and that a sizeable number of units (20.5%) had no policy. Although a very small minority (3.6%) did not allow any form of oral intake, most units permitted mothers to take either drink or food. A simple policy employed by approximately a third of units is to allow drinks to be taken by all mothers. Such a policy is easy to apply and does not cause confusion by the application of selection criteria. However, selection criteria were applied by approximately two-thirds of mater-

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Table 1. The Questionnaire.

Question 1:	Do you have a policy for oral intake during labour?
Question 2:	Are any mothers in established labour allowed drink or food?
Question 3:	If yes are mothers selected for drink or food?
Question 4:	If yes please show for the obstetric groups listed below, the operative risk category (low or high) to which mothers are allocated and the type of oral intake allowed (nil, drink or food). Primigravida Multiparous Grand multiparous Premature labour Breech/oblique/transverse Hypertension Pre-eclampsia Antepartum haemorrhage Bad obstetric history Prostin induction Artificial rupture of membranes/syntocinon induction Previous Caesarean section Small for dates Diabetes Other medical illness.
Question 5:	What drink do you give to mothers? The choices given were: water (including ice to suck), fruit juice, tea/coffee, soup and other.
Question 6:	What food do you give to mothers? The choices given were: toast, biscuits, low stomach residue diet and other.

Table 2. Oral intake policies.

	Yes	No	Total
Policy for oral intake during labour	221 (79.5%)	57 (20.5%)	278
Oral intake	268 (96.4%)	10 (3.6%)	278
drink only	180 (64.7%)		
drink and food	88 (31.7%)		
Selection for oral intake	183 (68.3%)	85 (31.7%)	268

nity units in England and Wales. In general, mothers with low risk allocation, such as uncomplicated primigravidae and multigravidae, were allowed oral intake, and those with high risk allocation, such as antepartum haemorrhage and abnormal lies, were not. Certain groups, such as the grand multiparous, demonstrated the wide difference of opinion expressed in our survey. The allocations for this group ranged from low risk/no oral intake to high risk/ food allowed. These differences highlight the contrasting positions taken on oral intake during labour despite the apparent lack of definitive knowledge on the subject.

Denying oral intake to labouring mothers with a high metabolic rate may deplete liver glycogen stores and induce ketoacidosis detrimental to mother and fetus. In contrast, some authorities argue that due to the shorter duration of labour nowadays mothers can manage without oral intake for a few hours.[8] However, Crawford demonstrated that even in mothers having forceps delivery, the most unplesant memory of their labour was the lack of drink and food.[9]

Despite extensive research on gastric emptying during labour and causes of maternal deaths, a relationship between oral intake and aspiration of gastric contents has yet to be shown. Nimmo and colleagues[6] demonstrated no delay in gastric emptying during normal labour, but a significant delay following the administration of opioid analgesics. Roberts and Shirley[10] showed that gastric volume increased after prolonged fasting and Magides and colleagues[11] found no difference in gastric emptying between the first, second and third trimesters of pregnancy. In a recent review of maternal deaths,[12] Morgan suggests that faulty anaesthetic technique is to blame for nearly all cases of maternal death due to aspiration of gastric contents. The report on maternal deaths[1] includes one case of aspiration pneumonitis despite prior administration of particulate antacids and H_2-receptor antagonists. Gastric emptying and pH were thought to be affected adversely by the administration of opioid analgesics during labour. Although particulate antacids may be implicated in the pathogenesis of the pneumonitis, combinations of nonparticulate compounds and H_2-receptor antagonists have failed occasionally to reduce gastric volume and increase

Table 3. Operative risk and oral intake according to obstetric group.

	Operative risk Oral intake					
	Low risk			High risk		
Mother group	Nil	Drink	Food	Nil	Drink	Food
Primigravida	0	125	44	1	5	0
Multiparous	0	128	48	0	0	0
Grand-multiparous	1	81	28	8	52	2
Premature labour	2	44	7	37	75	0
Breech/oblique/transverse	1	3	0	120	40	0
Hypertension	0	40	5	41	75	3
Pre-eclampsia	2	9	0	87	66	0
Antepartum haemorrhage	2	0	0	146	18	0
Bad obstetric history	0	13	1	70	77	1
Prostin induction	1	76	58	4	20	1
Artificial rupture of membranes/syntocinon induction	1	93	18	10	37	1
Previous Caesarean section	3	12	0	94	55	1
Small for dates	1	44	9	25	82	1
Diabetes	4	16	2	66	66	4
Other medical illness	0	25	4	22	67	2

Note: The numbers in individual rows do not total 183 due to void and nonapplicable answers.

Table 4. Nature of drink and food.

	Drink				
	Water	Fruit juice	Tea/coffee	Soup	Other
Number of units (Total 268)	268	47	121	45	10

Note: Other includes; cordial, milk, honey in hot water, dissolved sugar tablets, squash, build-up.

	Food			
	Toast	Biscuits	Low residue diet	Other
Number of units (Total 88)	76	48	32	28

Note: other includes; light diet, lollipop, ice cream, salad, sandwiches, jelly, normal diet, cereal, boiled sweets, sorbet, continental breakfast.

pH,[13] conditions that may potentially lead to aspiration pneumonitis. Therefore, it would be prudent to avoid the use of opioids in mothers who are at high risk for operative delivery and to promote the use of epidural analgesia.

A survey of institutional policies for oral intake in 448 American maternity units[14] showed that 28.1% of units had a nil per oris (NPO) policy, 18.9% allowed ice chips only and under 10% allowed food. Maternal mortality figures from aspiration of gastric contents in the United States are similar to those in England and Wales,[1,15] despite the much higher number of units employing an NPO policy compared to our study (3.6%).

A similar survey of 25 University affiliated maternity units in Canada[16] showed that most units allowed drinks, none allowed food and two had an NPO policy. Anaesthesia-related deaths accounted for 16% of total maternal deaths in Canada, compared to 12% in England and Wales for the same period.[14] Unfortunately, the Canadian figure did not specify those deaths attributed to aspiration of gastric contents.

A survey of labour ward routines used by consultant maternity units in England was conducted in 1984 by Garcia and Garforth.[17] Although details of any selection policy were not sought, the availability of drink and food allowed during labour was established. In our survey 68.3% of units did not allow food compared with 39% in the 1984 study. Food was allowed in established labour in 39% compared with 31.7% in our survey (1989). Water, and presumably any other form of oral intake, was not allowed by 2% of units in 1984 compared to 3.6% in 1989. Water, sips and ice cubes were given by 98% of units in 1984 and 96.4% in 1989. Other drinks were allowed by 67% of units in 1984 and 44% in 1989. Although not directly comparable, these surveys suggest that some changes have occurred during a 5 year interval. In 1989 fewer maternity units allowed food and drinks other than water to be taken. This change in policy may be due to the belief by some authorities that food and drink during labour is a contributory factor towards death from gastric aspiration or simply the result of the increased awareness of medicolegal implications.

In conclusion, this survey, in agreement with previous similar ones, demonstrates the inconsistency in current opinion on oral intake during labour. We believe that a rational approach, such as that advocated by Crawford[18] in relating risk allocation to oral intake, can be achieved. This highlights the need for further studies of risk and outcome in specific groups of mothers in labour. Until then policies for oral intake during labour will continue to show the great variation demonstrated by this survey.

Acknowledgments

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Postoperative pain control

A survey of current practice

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Summary

A survey of postoperative analgesia in 195 anaesthetic departments in England and Wales was undertaken. The results showed that 64% of respondents were dissatisfied or very dissatisfied with the present situation. Large differences were demonstrated between what was regarded as the safest technique and what would form the ideal management of postoperative pain.

Key words

Pain; postoperative.
Analgesia; patient controlled, epidural, intramuscular.

Following publication of the report 'Pain after Surgery' by a joint working party of the Royal College of Surgeons and the College of Anaesthetists,[1] there has been considerable interest in improving postoperative pain relief. This has centred round the development of High Dependency Units,[2] Acute Pain Teams[3] and expansion in the use of newer analgesic techniques such as patient controlled analgesia (PCA)[4] for larger numbers of patients. However, there is little information available about what is current practice in this country, making future audit of the impact of the working party report difficult. The present study set out to determine the current routine practice of anaesthetists, to assess what was regarded as ideal and safest practice and finally to assess anaesthetists' satisfaction with current management of postoperative pain.

Methods

A questionnaire was sent to the head of the department of anaesthesia in 195 hospitals in England and Wales. The hospitals chosen were those listed by the College of Anaesthetists as Schedule 1 or 2 for training. The participants were asked to consider their routine management of postoperative pain following major surgery; hemicolectomy and total hip replacement were given as examples.

The questionnaire asked the following.

Question 1: *Drugs routinely utilised peroperatively*
Participants were asked to select from a list of analgesics those that they routinely used peroperatively.

Question 2: *Drugs routinely utilised postoperatively*
This was similar to question 1 but enquired about the choice of postoperative analgesic.

Question 3: *Method of administration used routinely*
Participants were asked to select from a list those routes of administration they routinely used for postoperative analgesia.

Question 4: *Ideal method of administration*
Participants were asked to select from the list those methods they would use in ideal circumstances, defined as where there were no restrictions on equipment or nursing staff.

Question 5: *Safest method of administration*
Participants were asked to select which route they regarded as safest to use in the more normal situation i.e. a poorly staffed surgical ward.

Question 6: *Satisfaction with the current situation*
Participants were asked to grade their satisfaction with the degree of pain control in their postoperative patients on a four-point scale which ranged from very satisfied to very dissatisfied.

Results

One hundred and forty-six replies were received within 4 months of sending out the questionnaire, representing a return rate of 75%.

One hundred and forty-two respondents used opioids peroperatively, two of the remaining four used local anaesthetic drugs alone whilst the others reported using no specific peroperative analgesic. Table 1 displays the drugs used and the number of anaesthetists reporting their regular use. Thirty-four per cent of respondents use only one drug routinely, 33% use two, 19% use three and 10% use four.

Papaveretum is the most commonly used postoperative opioid, the incidence of use of the other drugs is shown in Table 2. Table 3 shows the current routine methods of administration of postoperative analgesia. Intramuscular injections on an 'as required' basis are still regularly used by 87% of those replying. Epidurals are used by 43%, PCA by 28%, closely followed by intravenous infusions (26%) and boluses (23%).

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Table 1. Peroperative analgesic: routine usage.

Drug	Number of units
Fentanyl	111
Papaveretum	70
Alfentanil	41
Morphine	35
Pethidine	21
Nalbuphine	7
Diclofenac	5
Phenoperidine	3
Levorphanol	3
Diamorphine	1
Cyclimorph	1
Buprenorphine	1
Methadone	1

Table 2. Postoperative analgesic: routine usage.

Drug	Number of units
Fentanyl	0
Papaveretum	118
Alfentanil	0
Morphine	57
Pethidine	53
Nalbuphine	3
Diclofenac	18
Phenoperidine	4
Levorphanol	3
Diamorphine	15
Cyclimorph	4
Buprenorphine	8
Methadone	1
Dihydrocodeine	1

Table 3. Current routine route of analgesic administration.

Route		Number of units	(%)
Intramuscular	Whenever necessary	127	(87)
	Regular	16	(11)
Intravenous	Bolus	34	(23)
	Infusion	38	(26)
	PCA	41	(28)
Subcutaneous	Bolus	2	(1)
	Infusion	11	(8)
Oral		11	(8)
Sublingual		7	(5)
Spinal	Local anaesthetic only	15	(10)
	Opioid only	6	(4)
	Combination	7	(5)
Epidural	Local anaesthetic only	22	(15)
	Opioid only	8	(6)
	Combination	33	(23)
Per rectum		3	(2)

Table 4 demonstrates what are regarded as the ideal routes of administration of postoperative analgesia. The intramuscular, oral, sublingual and subcutaneous routes were only suggested by 5% of respondents. The majority consider that PCA (58%) and the epidural (62%) routes are ideal.

Intramuscular 'as required' regimens for postoperative analgesia were considered the safest by 63% of respondents, while 18% felt that PCA was the safest. The other modes of delivery were considered safest by very few (Table 5).

Table 4. Ideal routes of analgesic administration.

Route		Number of units	(%)
Intramuscular	Whenever necessary		
	Regular	4	(3)
Intravenous	Bolus	9	(6)
	Infusion	40	(27)
	PCA	84	(58)
Subcutaneous	Bolus	1	(< 1)
	Infusion	1	(< 1)
Oral		1	(< 1)
Sublingual		1	(< 1)
Spinal	Local anaesthetic only	3	(2)
	Opioid only	14	(10)
	Combination	0	
Epidural	Local Anaesthetic only	7	(5)
	Opioid only	20	(14)
	Combination	63	(43)
Per rectum		0	

Table 5. Safest routes of analgesic administration.

Route		Number of units	(%)
Intramuscular	Whenever necessary	88	(63)
	Regular	0	
Intravenous	Bolus	1	(< 1)
	Infusion	1	(< 1)
	PCA	25	(18)
Subcutaneous	Bolus	3	(2)
	Infusion	3	(2)
Oral		6	(4)
Sublingual		6	(4)
Spinal	Local anaesthetic only	1	(< 1)
	Opioid only	1	(< 1)
	Combination	0	
Epidural	Local anaesthetic only	2	(1)
	Opioid only	3	(2)
	Combination	0	
Per rectum		0	

Table 6. Satisfied with current situation.

Very satisfied	1%
Satisfied	35%
Dissatisfied	61%
Very dissatisfied	3%

Finally, 64% of anaesthetists reported being dissatisfied or very dissatisfied with the current management of postoperative analgesia (Table 6).

Discussion

This study shows that the commonest analgesic technique is fentanyl given intravenously peroperatively, followed by an opioid drug such as papaveretum, given intramuscularly on a 'whenever necessary' basis for postoperative analgesia. Pharmacologically this technique can be seen to have several problems. Fentanyl can provide analgesia into the postoperative period when given in adequate doses, but it is known to have secondary peak effects[5] and can cause delayed respiratory depression.[6] It is well known that the respiratory depressant effect can continue for a considerable period after the analgesia has diminished[7] and that these effects are likely to occur when the patient is not

closely monitored, such as when he/she has been returned to the ward. A request for further analgesia will usually be managed by giving a longer acting opioid, usually papaveretum, by the intramuscular route. The patient has not received a loading dose of this drug and hence its duration of action and efficacy may be decreased just when the patient needs it most. Furthermore, the respiratory depression caused by this drug may be additive to that already present from the fentanyl. Further thought should be given to this commonly taught technique.

It is interesting to note that partial agonist drugs were not popular; only eight respondents used buprenorphine and three nalbuphine in the postoperative period. This is despite initial claims for these drugs of decreased problems with nausea, vomiting and respiratory depression and the attractiveness of the sublingual route of administration for buprenorphine.

Nonsteroidal drugs were included by 18 anaesthetists; the inclusion of hip surgery as one of the examples of major surgery in the questionnaire may well have influenced this result. However, their use seems to be increasingly popular as part of a balanced analgesic technique following major abdominal surgery.

Our results demonstrated that 87% of anaesthetists routinely use intramuscular 'whenever necessary' regimens for postoperative analgesia; this compares with the 52% reported in other recent surveys of anaesthetic practice.[8] However, intravenous infusions (26%) and PCA (28%) were reported to be used routinely by relatively large numbers of respondents. It is also interesting to note that a number (23%) use combinations of opioids and local anaesthetic agents epidurally; this compares with figures for the use of such combinations in the USA and Sweden of 59% and 94% respectively.[9,10]

In ideal circumstances most anaesthetists would abandon the traditional intramuscular regimen in favour of intravenous and epidural routes of administration. Fifty-eight per cent consider PCA, and a further 27% intravenous infusions, as ideal. This represents a doubling of the number of respondents considering PCA, with little change in the advocates of intravenous infusions. Epidural analgesia was favoured by 62% of anaesthetists compared to only 43% using them at present. It will be noted that this increase was both in respondents wishing to use opioids alone and those wishing to use these in combination with local anaesthetic agents.

When asked to consider the safest technique to use in poorly staffed postoperative wards, respondents showed a considerable shift; 63% supported the use of intramuscular 'whenever necessary' regimens. Eighteen per cent believed that PCA was still appropriate and very few felt that there was any indication for the other techniques. This result showed a marked change from the 'ideal' situation but also, surprisingly, a major deviation from current practice. It is interesting to note that the intramuscular 'whenever necessary' regimen is considered safest, but recent oximetry studies performed on postoperative patients utilising a selection of analgesic regimens challenge this view.[11] The change from reported current practice could be partly explained if those using intravenous infusions and epidural delivery of drugs do so in High Dependency or Intensive Care Units. Some of the comments on the questionnaire would support this; 10 of the 38 respondents reported routine use of intravenous infusions, stating that they did this in an ITU/HDU environment.

Overall, 64% of respondents were dissatisfied or very dissatisfied with their present management of postoperative pain.

In conclusion, there appears to be support for the joint colleges' report about the management of postoperative pain. However, there is some considerable way to go before anaesthetists will be satisfied with both the degree and safety of postoperative analgesia.

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Day case laparoscopy: a survey of postoperative pain and an assessment of the value of diclofenac

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Summary

A randomised, controlled study was undertaken to assess the postoperative pain and side effects experienced by patients undergoing day case diagnostic laparoscopy and laparoscopic sterilisation, and to evaluate the effectiveness in these patients of peroperative diclofenac. Patients undergoing laparoscopic sterilisation had significantly higher pain scores at one hour postoperatively, and at discharge, than patients undergoing diagnostic laparoscopy ($p < 0.01$) but there were no significant differences in pain scores 24 hours after discharge. The incidence of postoperative side effects following discharge from hospital was high, but there were no significant differences between the groups. Diclofenac had no significant effect in either group on the severity of postoperative pain, or the incidence of postoperative side effects.

Key words

Analgesia; postoperative.
Analgesics; diclofenac.
Surgery; laparoscopy, outpatient.

Day case surgery offers many potential advantages for both patients and hospital services. Diagnostic laparoscopy and laparoscopic sterilisation are regularly performed on a day case basis. However, the incidence of postoperative sequelae is high,[1] and postoperative pain relief can be difficult to achieve, particularly after laparoscopic sterilisation.[1,2] The aim of this study was to compare the levels of postoperative pain and other side effects experienced by patients undergoing both types of surgery and to assess the value of peroperative intramuscular diclofenac.

Methods

The study was approved by the local Hospital Ethics Committee, and informed consent was obtained from each patient. Equal numbers of patients, ASA grades 1 or 2, undergoing diagnostic laparoscopy or laparoscopic sterilisation as day cases were recruited to the study. Patients with known allergy to any of the drugs to be used, or a history of bronchial asthma or peptic ulceration, were not studied. All patients received a standard anaesthetic. No premedication was used. Anaesthesia was induced with propofol (2.5–3 mg/kg) and intubation and intermittent positive pressure ventilation facilitated by vecuronium (0.07 mg/kg). Anaesthesia was maintained with isoflurane 1% in 33% oxygen and 66% nitrous oxide. At the end of the procedure, neuromuscular blockade was reversed with neostigmine (3.75 mg) and glycopyrronium (0.75 mg).

The patients were randomly allocated to receive either an intramuscular injection of diclofenac (75 mg) immediately following induction of anaesthesia, or no injection. This resulted in four groups of patients: group 1 (diagnostic laparoscopy control), group 2 (diagnostic laparoscopy plus diclofenac), group 3 (laparoscopic sterilisation control), and group 4 (laparoscopic sterilisation plus diclofenac).

In the postoperative period, analgesia was given by the nursing staff on request from the patient. Initially, analgesia was provided with paracetamol (1 g). If further analgesia was requested, co-proxamol (2 tablets) was given. If following this, analgesia was still inadequate, intramuscular pethidine was given, and the patient admitted for overnight hospital stay.

Postoperative recovery was assessed by measuring the time taken for patients to open their eyes, and to state correctly their name and address.

Patient self assessment of pain was performed after return to the ward, using a 10 cm visual analogue pain scale (VAS). The assessments were made in the presence of an independent observer, who was unaware as to whether the patient had received diclofenac. These assessments were performed immediately on return to the ward, one hour after return to the ward, and just prior to discharge. On discharge, patients were also questioned about the presence and severity (absent, mild, severe) of the following symptoms: nausea, headache, sore throat, giddiness, tiredness and shoulder pain. All patients were given a questionnaire to complete at home which contained a 10 cm VAS to assess their pain at 24 hours after discharge, and questions on the incidence of side effects during the following 48 hours after discharge. They were also asked how long it took before they could resume normal activities, and whether or not they would be prepared to undergo the same operation as a day case patient again. Patients who were admitted to hospital overnight were also asked to complete the questionnaire at 24 hours after their operation.

Statistical analysis. Patients' age, weight, the duration of surgery and recovery time, were analysed using Student's *t*-test. Analgesic requirement and pain scores were analysed using the Mann–Whitney *U*-test.

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Table 1. Characteristics of the groups, mean (SD).

	Group 1 DL control $n = 20$	Group 2 DL+diclofenac $n = 20$	Group 3 LS control $n = 20$	Group 4 LS+diclofenac $n = 20$
Age; years	30.0 (6.7)	27.9 (6.1)	*33.2 (6.0)	*33.3 (5.2)
Weight; kg	62.5 (6.4)	59.1 (8.0)	60.1 (8.6)	61.3 (8.7)
Operating time; minutes	17.4 (2.5)	18.3 (4.0)	17.6 (3.0)	16.5 (4.4)
Eye opening; minutes	4.1 (1.4)	4.8 (1.6)	3.8 (1.8)	4.8 (1.9)
State name and address; minutes	6.4 (1.8)	6.5 (1.5)	6.5 (2.1)	7.1 (1.6)

DL, diagnostic laparoscopy; LS, laparoscopic sterilisation.
*$p < 0.01$ compared to group 2.

Table 2. Postoperative side effects before discharge (number of patients).

		Group 1 $n = 20$	Group 2 $n = 20$	Group 3 $n = 20$	Group 4 $n = 20$
Nausea	none	13	15	9	9
	mild	7	4	6	9
	severe	0	1	5	2
Headache	none	15	17	17	18
	mild	4	2	3	2
	severe	1	1	0	0
Sore throat	none	8	7	14	16
	mild	12	9	6	4
	severe	0	4	0	0
Giddiness	none	18	14	16	13
	mild	2	5	4	7
	severe	0	1	0	0
Tiredness	none	6	9	10	6
	mild	10	9	8	12
	severe	4	2	2	2
Shoulder pain	none	13	11	12	14
	mild	5	5	4	4
	severe	2	4	4	2

Table 3. Postoperative side effects in the 48 hours after discharge (number of patients).

		Group 1 $n = 18$	Group 2 $n = 14$	Group 3 $n = 14$	Group 4 $n = 16$
Nausea	none	11	8	10	11
	mild	6	6	3	3
	severe	1	0	1	2
Headache	none	12	10	13	14
	mild	5	4	1	2
	severe	1	0	0	0
Sore throat	none	3	2	8	8
	mild	13	10	5	7
	severe	2	2	1	1
Giddiness	none	10	9	13	10
	mild	7	4	0	5
	severe	1	1	1	1
Tiredness	none	2	1	5	5
	mild	12	11	7	7
	severe	4	2	2	4
Shoulder pain	none	4	4	5	5
	mild	5	3	5	8
	severe	2	7	4	3

Table 4. Postoperative pain (mean (SEM)).

Time of pain score	Group 1 $n = 20$	Group 2 $n = 20$	Group 3 $n = 20$	Group 4 $n = 20$
Immediately on return	46.2 (5.3)	44.1 (5.5)	70.1 (4.0)	56.9 (4.0)
At 1 hour	25.0 (3.3)	25.6 (4.5)	60.8 (4.3)*	52.8 (5.6)**
On discharge	17.0 (2.9) $n = 18$	19.2 (4.7) $n = 14$	54.8 (5.6)* $n = 11$	47.9 (6.8)** $n = 12$
At 24 hours	38.1 (4.4)	41.2 (6.0)	49.6 (9.5)	39.5 (8.7)

*$p < 0.001$, when group 3 is compared with either group 1 or 2.
**$p < 0.001$, when group 4 is compared with group 1; $p < 0.01$, when group 4 is compared with group 2.

Table 5. Postoperative analgesic requirement (number of patients).

Analgesia required	Group 1 $n = 20$	Group 2 $n = 20$	Group 3 $n = 20$	Group 4 $n = 20$
None	11	13	2	1
Paracetamol	9	7	6	13
Paracetamol plus coproxamol	0	0	9	2
Pethidine	0	0	3	4

group 3 > group 1 and group 2; $p < 0.001$.
group 4 > group 1; $p < 0.001$.
group 4 > group 2; $p < 0.01$.

Results

A total of 80 patients (four groups of 20) participated in the study. Patients in groups 3 and 4 were slightly older than those in group 2 ($p < 0.01$), but there were no other significant differences between the groups in respect of age, weight, duration of surgery or recovery times (Table 1).

Table 2 shows the incidence of postoperative side effects on discharge. There were no significant differences between any of the groups. Only 62 (78%) out of 80 'take home' questionnaires were returned; the results are shown in Table 3. There were no significant differences between any of the groups.

Tables 4 and 5 show the severity of postoperative pain and analgesic requirements. There were no significant differences between the two diagnostic laparoscopy groups (1 and 2), or between the two laparoscopic sterilisation groups (3 and 4). However, patients in the sterilisation groups had significantly greater pain scores than those in the diagnostic groups, both at one hour and at discharge. They also required significantly more analgesia postoperatively.

No patients from groups 1 or 2 required overnight admission. Three patients from group 3, and four from group 4 were admitted for pain relief. Two other patients were admitted from group 4, one because of extreme tiredness and one for social reasons.

All groups of patients had high pain scores 24 hours postoperatively (scores of patients who had required admission are not included). There were no differences between the groups in either the site, or the severity, of the pain (Table 4). No patients contacted the hospital with any problems, but one patient in group 3 felt it necessary to contact her General Practitioner on the first postoperative day for stronger analgesic therapy, and another patient from group 3 fainted whilst at home. It took patients an average of 36 hours to return to normal activities after discharge.

Of the patients who returned their questionnaire, 78% of diagnostic laparoscopy patients and 70% of laparoscopic sterilisation patients would have been prepared to undergo the operation as a day case again.

Discussion

We have shown that in the immediate postoperative period, patients undergoing laparoscopic sterilisation suffered more pain than patients undergoing diagnostic laparoscopy. Twenty-four hours after discharge, day case laparoscopy patients still had pain sufficient to limit their activities, but by this time there was no difference in the degree of pain experienced by the two operative groups. Diclofenac did not significantly reduce the severity of the pain experienced, or analgesic requirement, following either operation. These results are disappointing, as diclofenac has been shown to be as effective as opioids in treating pain in a wide variety of situations.[3–7]

The actual cause of the pain after laparoscopy is obscure. The higher initial pain scores of sterilisation patients is probably due to the presence of the Filshie clips on the Fallopian tubes, causing either a direct pressure effect, or possibly tubal spasm. The similarity in the degree of pain suffered by all groups at 24 hours, and the high incidence of shoulder pain, would suggest that pain experienced at this time may be related to either the patient's head-down position on the operating table, or the diaphragmatic stretching and irritation caused by the carbon dioxide gas used for insufflation.

The high incidence of other postoperative symptoms was similar to that shown by Collins *et al.*;[1] sore throat and tiredness were particularly troublesome. Diclofenac has been shown to reduce the incidence of minor postoperative symptoms in dental day case surgery,[5] but we have not shown a similar effect in this group of patients.

As pressure to perform surgical procedures on a day case basis increases, it is important to maintain a high standard of patient care. We have demonstrated a high occurrence of minor postoperative complications, and significant postoperative pain associated with day case laparoscopy, parti-

cularly after laparoscopic sterilisation, which was not significantly improved by intramuscular diclofenac. Seven out of 40 patients who had laparoscopic sterilisation required overnight admission for pain relief and we feel that this calls into question the suitability of this operation for day case surgery. Certainly, such operations should be performed early in the day, and facilities for hospital admission should be available. Despite this, we were encouraged that more than 70% of patients undergoing either operation would be happy to be a surgical day case patient again. We feel that the search for measures to reduce postoperative sequelae in these patients must continue.

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Anaesthesia, 1991, Volume 46, pages 1081–1094

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Quality of anaesthesia during spontaneous respiration: a proposed scoring system

Scoring systems are available for the assessment of recovery following anaesthesia,[1,2] but little attention has been given to the evaluation of the quality of anaesthesia achieved during the maintenance period. Evans and Davies[3] have proposed a scoring system to assess the adequacy of anaesthesia based on four clinical signs: blood pressure, heart rate, sweating and tears (PRST score) and have advocated the use of the score to assist in the control of anaesthesia in an individual patient. In certain areas of clinical research in anaesthesia, there could be an advantage in attributing a quality score to an individual anaesthetic procedure. Such a score would allow an evaluation of the effect of experience with any given technique on the quality of anaesthesia achieved. Mean scores from groups of patients could be useful in comparing the quality of anaesthesia obtained with different analgesics, hypnotics or inhalational agents.

In the spontaneously breathing patient, four interrelated factors influence the overall assessment of the maintenance period. A scoring system is proposed (Table 1) in which optimum conditions are indicated by a lack of response to surgical stimulation, acceptable effects on respiration and circulation and rapid recovery following termination of anaesthetic administration. The assessment begins with an

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Table 1. Quality of anaesthesia score.

(A) *Movement in response to surgical stimulation*	
None	10
Occasional mild response (no interruption to surgery)	12
Frequent mild response	15
Occasional marked response (temporary interruption to surgery)	18
Frequent marked response	20
(B) *Haemodynamic instability*	
None (MAP 75-110), HR < 91	0
Occasional tachycardia (HR > 90) hypertension (MAP > 110) or hypotension (MAP < 75)	1
Persistant marked hypotension (MAP < 75)	2
Frequent or persistent tachycardia (HR > 90) or hypertension (MAP > 110)	3
(C) *Mean end-tidal CO_2 (kPa)*	
4.0–5.9	0
6.0–7.3 or < 4.0	1
7.4–8.6	2
> 8.6	3
(D) *Recovery time from end of surgery to eyes open on command*	
< 5 minutes	0
5–10 minutes	1
11–20 minutes	2
> 20 minutes	3

Total score: A. Movement [ ] (12–20) +B [ ] +C [ ] +D [ ] or A. No movement [10] −B [ ] −C [ ] −D [ ] = [ ]

overall evaluation of movement in response to surgery. Thereafter the other aspects are scored and where movement has been observed, the scores in these areas are added to the movement score. Where no movement is observed, these secondary scores are subtracted from the movement score. Thus achievement of optimum conditions provides a score of 10.

Effects associated with light anaesthesia result in positive increments, whereas deep anaesthesia accompanied by respiratory depression and resulting in delayed recovery would produce a smaller score.

To promote consistency, a number of further definitions are proposed: (1) to provide a total score for an individual procedure, a single, worst case score should be allocated for each of the four aspects, based on an overall assessment of the period of maintenance; (2) the assessment period over which the first three aspects are evaluated should run from 10 minutes following induction until the end of anaesthetic administration; (3) for comparative studies, inclusion and exclusion criteria should be considered carefully. The system would not be appropriate for patients with hypertension and could be influenced by ancillary drugs, which may effect the cardiovascular system or affect recovery time. The operative procedure, or degree of surgical stimulation, would also need to be standardised; (4) a response to surgical stimulation at any time within the assessment period should be noted. Responses should be classed as occasional if one or two are noted over a 60 minute period, over the total period for shorter procedures, and frequent or persistent if more than two are observed over this interval; (5) the assessment of haemodynamic instability is the most difficult area. If heart rate and MAP are recorded at 5 minute intervals, 'occasional' and 'frequent' could be defined as above, but relating to the number of 5 minute readings occurring outside the set limits. While percentage changes from baseline would be more valuable,[4,5] absolute values of MAP and heart rate are preferred for reasons of simplicity. A visual assessment can be made by placing a scaled, transparent template over a standard anaesthetic chart; (6) the measurement of end-tidal CO_2 is intended to provide an average value during stable anaesthesia rather than to monitor acute changes in response to inadequate anaesthesia. It is envisaged that end-tidal monitoring could be facilitated with a laryngeal mask or with a tracheal tube placed after the administration of a short acting neuromuscular blocking drug. If end-tidal monitoring is not achievable, the system could probably be amended to score respiratory rate in an equivalent manner.

It is recognised that many factors related to the overall success of a given procedure are not taken into account at present. Events occurring at induction or during emergence and factors such as postoperative comfort has not been included.

The purpose of this communication is to invite comment and hopefully to stimulate research in this area. In this way the sensitivity of the proposed system may be evaluated and modifications and improvements devised. I am grateful for the comments and suggestions received to date from a small number of anaesthetists with whom this general concept has been discussed.

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Laryngeal mask airway for coronary artery bypass grafting

We would like to respond to the letter from Drs Foster and Clowes (*Anaesthesia* 1991; **46:** 701). For brevity, in our previous letter (*Anaesthesia* 1991, **46:** 234) we did not expand on this case; however, we would state that, apart from airway management, this case was carried out in our normal way. It is our practice to extubate patients' tracheas when they are stable. In our unit the median duration of ventilation is 60 minutes and the median time to extubation 2 hours. Seventy-two percent of patients are self-ventilating at 2 hours, and 53% have been extubated by this time. We are fortune that in our unit, the cardiac recovery ward is part of the operating theatres and one or more of the authors are immediately available for postsurgical management.

Whilst we too would not defend the use of the laryngeal mask airway in an ITU where staff are unfamiliar with it, we would like to point out that tracheostomy prior to sternotomy and cardiopulmonary bypass with heparinisation is not without complication, and should not be undertaken lightly. The long-term complication of mediastinal sepsis associated with early tracheostomy is also well recognised.

As in all instances, the anaesthesic technique used must depend on the patient, personnel, and facilities available.

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Laryngeal mask and gastric dilatation

As use of the laryngeal mask airway (LMA) increases, so will the variety and incidence of the complications. We report two cases of gastric dilatation associated with intermittent positive pressure ventilation (IPPV) and the LMA.

Case 1 was a 44-year-old woman, weight 62 kg and ASA 1, who presented for total abdominal hysterectomy. Premedication was with pethidine 100 mg and atropine 0.6 mg an hour pre-operatively. Induction was with propofol 2.5 mg/kg, followed by tubocurarine 30 mg and diclofenac 75 mg intramuscularly. After gentle manual inflation of the lungs with nitrous oxide and oxygen, a size 3 LMA was easily passed and the cuff inflated with 20 ml air to make an airtight seal. A Manley pulmovent MPD 200 was then used with a ventilation pressure less than 20 cmH_2O and tidal volume 600 ml to achieve a $P\text{CO}_2$ of 4 kPa. The operation was uneventful until the abdominal retractor was withdrawn to close the peritoneal cavity. It was then noted that the stomach was grossly dilated making closure impossible. A nasogastric tube was passed and the stomach deflated rapidly.

Case 2 was a 32-year-old woman, weight 66 kg and ASA 1, for diagnostic laparoscopy. Premedication and anaesthesia were similar to the above except that vecuronium 5 mg (0.76 mg/kg) was used for muscle relaxation. A size 3 LMA was passed easily and the cuff inflated with 25 ml of air. The peritoneal cavity was insufflated with CO_2 to 3 litres, following which the stomach was found to be grossly distended to below the umbilicus. Insertion of the trochar into the peritoneal cavity would have put the stomach at risk of perforation. A nasogastric tube was passed and the stomach emptied easily; the operation then proceeded normally.

A search of the literature did not reveal previous case reports of gastric dilatation as a complication of IPPV with the LMA. However, the instruction manual[1] warns of the possibility of gastric dilatation due to malposition of the mask, the use of unnecessarily high inflatation pressures or large tidal volumes. In both these cases a size 3 mask, which is recommended for small adults over 25 kg, was used. However both women weighed more than 60 kg and it may be that a size 4 mask would have been more appropriate. Since these cases, a size 4 mask is now selected for most adults.

In conclusion, IPPV can be used successfully with the LM providing the proper precautions are observed and the possibility of gastric dilatation is borne in mind.

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Laryngeal mask to aid tracheal intubation

We read with interest the technique for awake intubation developed by McCirrick and Pracilio, (*Anaesthesia* 1991; **46:** 661–3) using the laryngeal mask airway (LMA). We have found a similar technique useful. This technique differs in a number of ways: adequate anaesthesia of the pharynx, larynx and trachea is obtained using topical and transtracheal 4% lignocaine. A catheter mount with suction port is attached to the LMA to allow the patient to breathe spontaneously gas supplied from an anaesthetic machine. A hollow bougie-like introducer is then inserted into the larynx via the self-sealing suction port. Correct placement of the introducer in the larynx can be confirmed by measurement of carbon dioxide efflux from the introducer by connecting it to a standard end-tidal CO_2 monitor.

We feel this technique offers a higher success rate than that reported by Alison and McCrory.[1] It also allows the patient to continue breathing 100% oxygen or whatever mixture of gases and volatile agent required.

At present we are completing a series of awake intubations to determine the success rate and the incidence of desaturation, laryngospasm, and vomiting.

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Intra-operative airway maintenance for short ophthalmological procedures in children

Anaesthesia for short ophthalmological procedures in children presents several difficulties. Mask anaesthesia causes problems for the surgeon in terms of access, while deep anaesthesia followed by removal of the mask limits the time of surgical access. Tracheal anaesthesia has its own disadvantages for such short procedures.[1,2] Although ketamine allows easy maintenance of the airway it has been found to have undesirable effects.[3,4]

We have modified a Guedel oropharyngeal airway with a Jackson–Rees attachment of a paediatric T-piece in an effort to improve upon the existing techniques. Bite blocks of 00, 0, 1 and 2 size Vygon Guedel airways were removed and in their place Magill's nasal tracheal tube connectors, numbers 11, 12, 12 and 12 respectively were inserted, which fitted snugly. This was connected to the patient end of a Jackson–Rees attachment by a soft, light weight, flexible and short corrugated rubber connector (Fig. 1).

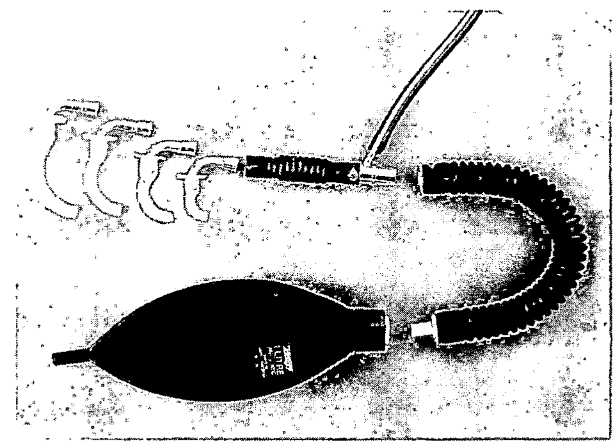

Fig. 1.

The technique was used in 30 unpremedicated children aged 3 months to 10 years after obtaining institutional approval and informed parental consent. The surgical procedures ranged from 8–50 minutes. Anaesthesia was induced with 60% nitrous oxide and 1.5 to 2% halothane in oxygen via a facemask. Intravenous access was established and pethidine 1 mg/kg and promethazine 0.5 mg/kg was administered. After ensuring jaw relaxation and abolition of the gag reflex, the modified Guedel oropharyngeal airway assembly was introduced and the flange fixed with the help of an adhesive plaster. The head, resting on a support, was kept slightly extended at the atlanto-occipital joint. Facilities for tracheal intubation were always kept at hand. The anaesthetic course was uneventful in all the cases. The maximum concentration of halothane required never exceeded 2% and the children tolerated the airway and the surgery very well. Partial respiratory obstruction was observed in six children and was effectively relieved by chin support. No nausea or vomiting were encountered during or after the procedure. The surgeon has an uninterrupted field as the breathing system lies toward the lower part of the body with the Magill's connector fixed on the chin. Air dilution is not a problem because the tip of the airway lies in the posterior pharynx and the flow is always kept adequate. Precautions which should be taken are putting in the assembly when the gag reflex is abolished, watching carefully the movements of the reservoir bag, support of the chin if partial or complete respiratory obstruction occurs and removing the assembly at the proper time.

From our experience we feel this to be a simple, safe and practical method needed for short ophthalmological procedures in children, especially in day care situations.

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Oral ketamine

We have had experience with oral ketamine in over 80 children undergoing cardiac surgery and were interested to read of its use in mentally retarded adults undergoing dental treatment (*Anaesthesia* 1991; **46:** 646–7) and would like to share our observations from a pilot study of 40 children.

We assessed sedation, cooperation with induction, salivation and cardiovascular and respiratory effects of oral ketamine 5 mg/kg and 10 mg/kg (20 patients in each group, mean age 33 months, SD 23 months) and some results are given in the Table. Sedation was satisfactory in 75% with 5 mg/kg and 90% with 10 mg/kg, 1 hour after administration. Cooperation with induction was excellent: intravenous cannulation was accepted by 95% and it was possible to perform radial arterial cannulation in eight patients after the 10 mg/kg dose because, although they were awake, they were passive and did not struggle or require restraint. However, it was obvious that these patients were 'dreaming' and hyperventilating. Arterial blood gas analysis showed that of the 40 patients, 38 were moderately and two extremely hypocarbic. The higher dose of ketamine was associated with increased salivation, which

Table 1. Sedation after oral ketamine.

		5 mg/kg	10 mg/kg
Asleep and rousable	satisfactory	1	4*
Awake and calm	satisfactory	14	14
Awake and anxious	unsatisfactory	4	1*
Upset	unsatisfactory	1	1
Salivation			
Normal		14	4†
Moderate		4	13†
Excessive		2	3

*p < 0.05 Kendall-tan test.
†p < 0.01 Chi-square test.

OXYGEN %

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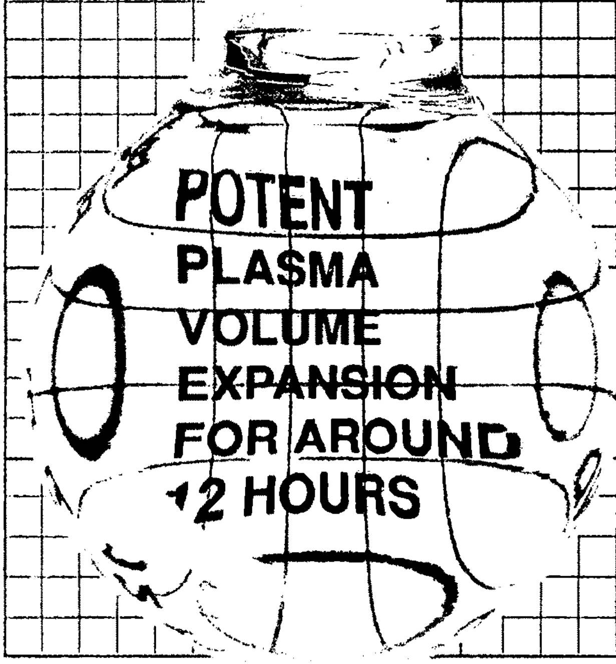
	170
Heart rate	160
	150
	140
	130
Temp	120
	110
	100
	90
	80
	70
	60
	50
	40
	30
	20
	10
	0



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was excessive in 12.5% overall. Three patients exhibited abnormal movements after premedication, one following the smaller dose. There were no significant changes in heart rate, blood pressure or arterial oxygen saturation. Ketamine alone has a foul taste, but it was well accepted when disguised in orange juice, although one vomited 45 minutes later.

The pharmacokinetics of oral ketamine and its metabolite norketamine are interesting. Although the bioavailability of oral ketamine is low at 16.5%, the peak plasma norketamine levels are much higher than those after the same dose intramuscularly.[1] Norketamine probably has anaesthetic and analgesic properties and this possibly accounted for the remarkable lack of response to venepuncture or arterial cannulation.

We were attracted by the analgesic and sedative effects of oral ketamine, but the salivation, hypocarbia and dreaming were undesirable side effects in our patients. Eventually, we returned to more conventional premedicant drugs because of disquiet due to the passivity and abnormal movements, but not before combining oral trimeprazine and oral ketamine which rectified the salivation and hyperventilation.[2]

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Ketamine and propofol for TIVA

We would like to comment on the paper by Guit *et al.* (*Anaesthesia* 1991: **46:** 24–7). The infusion rates of propofol and ketamine are similar to the rates that we have used in the spontaneously breathing patient for peripheral surgery, such as debridement of wounds, below knee amputation and formation of arteriovenous fistulae. Because of the low infusion rate of ketamine and the interpatient variability to the effects of most drugs, how did they know that they did not have inadequate analgesia or hypnosis in a paralysed patient?

Following premedication with oral lorazepam, our patients were given glycopyrroninm to reduce secretions and anaesthesia was induced with ketamine 1 mg/kg and initially propofol 2 mg/kg, which we have now reduced to 1 mg/kg. Ketamine was then infused at 3 mg/kg/hour, and the propofol as per the regimen of Richards *et al.*[1] An air/oxygen mixture was breathed through a medium concentration oxygen mask.

A transient apnoea occurred at induction but on recovery from this the patients were able to maintain their airway. Heart rate increased slightly after the glycopyrronium (a mean of 7 beats/minute), but increased by a mean of 18 beats/minute after induction of anaesthesia. Subsequently the heart rate remained stable. Mean arterial blood pressure fell on average by about 5 mmHg. In two patients nonspecific limb movements occurred, unrelated to any surgical stimulus, and could not be controlled by additional propofol. The time taken to full recovery was very variable and independent of patient factors or duration of surgery. All patients were comfortable in the immediate recovery period and some felt intoxicated. Two patients experienced dreams, but they were not unpleasant. We have further refined this technique using other nonopioid analgesics (nefopam and tenoxicam) and this has improved the cardiovascular stability. As an aside, an attempt was made to reduce the rate of infusion of ketamine below 3 mg/kg/hour. This proved to be unsatisfactory as the patients lost control of their airway; it seems likely that a critical concentration of ketamine is required to maintain the muscle tone in opposition to the propofol.

What data gave Guit *et al.* the confidence that their technique was free from the danger of awareness prior to the study? Our patients were able to move in response to noxious stimulation if insufficiently anaesthetised. We believe that the propofol/ketamine/nonopioid analgesic combination is a fruitful avenue for total intravenous anaesthesia investigation.

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A reply

Thank you for the comments. Penberthy and Harrison used the propofol/ketamine combination as total intravenous anaesthesia in spontaneously breathing patients. Compared to our study, the administered dose of propofol was lower and the dose of ketamine higher. The occurrence of nonspecific limb movements unrelated to any surgical stimulus and not reacting to additional dose of propofol has raised the question of awareness in these patients. However, these movements can also be explained by the choice of the drugs; involuntary movements are reported in 17% of patients during infusions of propofol[1] and in 16% of patients older than 30 years during ketamine anaesthesia.[2]

It was precisely to avoid the possibility of awareness that we chose an infusion scheme for propofol which was higher than that reported to be adequate for surgical anaesthesia. The mean blood level of propofol required for adequate hypnosis during anaesthesia has been estimated to be 2.42 μg/ml (SD 0.43)[3] and a blood level above 3 μg/ml is considered to be adequate to maintain surgical anaesthesia.[4] An infusion scheme consisting of a loading dose of 1 mg/kg propofol, followed by an infusion of 10 mg/kg/hour for 10 minutes, 8 mg/kg/hour for the next 10 minutes and 6 mg/kg/hour therafter, is reported to produce overall mean blood propofol concentration of

3.67 μg/ml within 2 minutes, which remains stable during surgery.[4] Other studies have reported no awareness in patients anaesthetised with this infusion scheme.[5,6] Our infusion scheme consisted of a loading dose of 2 mg/kg propofol, followed by an infusion of 12 mg/kg/hour for 30 minutes, 9 mg/kg/hour for the next 30 minutes and then 6 mg/kg/hour. None of the patients reported awareness.

In our study ketamine was used as the analgesic for total intravenous anaesthesia with propofol. The dosage rate of ketamine was the same as that reported previously in combination with midazolam.[7] Increments of analgesics were given during anaesthesia if analgesia was judged clinically to be inadequate, as assessed by a sudden increase of systolic blood pressure of more than 20 mmHg, an increase in heart rate of more than 10 beats/minute in absence of hypovolaemia and signs of sweating and lacrimation. None of the patients in the propofol/ketamine group received additional doses of ketamine.

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Prolonged apnoea, trismus and ketamine

Although claimed to be safe for emergency anaesthesia, ketamine has the potential to depress the pharyngeal and laryngeal reflexes. Pulmonary aspiration has occurred following ketamine anaesthesia.[1] Hypertonus of skeletal muscles after ketamine may occur upto the extent of airway obstruction and apnoea.[2] We report a situation where apnoea and trismus occurred simultaneously following intramuscular ketamine.

A 6-year-old, 20 kg boy presented with an injury over the left eyebrow requiring stitches. Respiratory and cardiovascular parameters were normal without any sign of raised intracranial or intra-ocular pressures. The child was very cooperative and a local anaesthetic was planned. Diazepam 5 mg and promethazine 25 mg were given intramuscularly and 30 minutes later he was mildly sedated. However, he became uncooperative during transfer to the operating theatre and local anaesthetic was deemed unsafe. He refused an injection of ketamine and therefore 70% N_2O in oxygen with halothane was administered for sedation, prior to intramuscular ketamine 6 mg/kg and atropine 0.3 mg. All other agents were then withdrawn and he breathed room air. Ten minutes later, all vital signs were stable and surgery commenced. However, within 5 minutes the child suddently became apnoeic. Attempts to introduce a Guedel airway failed due to intense spasm of the jaw muscles, although the limbs remaining flaccid. Artificial ventilation with bag and mask failed due to an obstructed airway and he become cyanotic. In view of the rapid fall in pulse rate and $Sa{O_2}$ and while suxamethomium was being prepared, blind nasal intubation was attempted which was successful. Artificial ventilation was commenced with 100% oxygen. Both pulse rate and $Sa{O_2}$ returned to their precyanotic levels almost immediately.

Once $Sa{O_2}$ was regained, the ventilating gas was converted to 70% N_2O in oxygen. Surgery was completed within 20 minutes. Artificial ventilation had to be continued until return of spontaneous respiration after 45 minutes, but the trismus lasted for a further 20 minutes. After breathing spontaneously for 10 minutes, his trachea was extubated. No cutaneous sign of an allergic reaction was evident at any stage. Further recovery was uneventful.

Use of high dose ketamine in infants required for lack of movement, has been associated with respiratory depression and apnoea, particularly in those with a raised intracranial pressure.[3] In this patient no evidence of raised intracranial pressure was present, and the dose of ketamine was lower than that usually recommended. We are of the opinion that ketamine was responsible for the apnoea, trismus and depressed laryngeal reflexes in this patient. Promethazine is claimed to be a depressant of upper respiratory tract reflexes[4] and probably accentuated the ketamine-induced suppression. The fact that the trismus outlasted the apnoea suggests a separate aetiology, although both remain unexplained.

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The oesophageal detector device

I would like to thank Dr Baraka (*Anaesthesia* 1991, **46:** 697) for drawing to our attention three cases where the oesophageal detector device (ODD) in the form of a self-inflating bulb reflated only very slowly in two cases and not at all in one, even though in all three cases the tracheal tube was placed in the trachea. In two of the cases there was

external tracheal compression by a large thyroid gland and a lymphoma respectively. In the original clinical trial,[1] it was emphasised that the ODD was tested only in patients with normal oesophageal or tracheal anatomy. It was suspected that distortion of anatomy could lead to misleading results since the principle of the ODD relies on the differences between the trachea and the oesophagus.

On this basis, it was surprising to read of Dr Baraka's report that very slow reflation of the ODD occurred in an asthmatic patient. In asthma, bronchoconstriction occurs predominantly in the smaller airways. Since the ODD does not rely on the patency of the smaller airways as opposed to the trachea, it would seem to be the ideal device for detecting tracheal intubation where auscultation or decreased reservoir bag compliance may make confirmation of tracheal intubation more difficult during bronchospasm. In the original study,[1] two cases of moderate bronchospasm, where the maximum airway pressures were between 3.0 and 4.2 kPa, did not present any difficulty for the observers to detect tracheal tube placement.

There are several explanations for slow reflation of the bulb when the tracheal tube is in the trachea. Bronchial intubation,[1] the tracheal tube filled with secretions[1] or the posterior placement of the bevel of the tracheal tube against the tracheal wall[2] may all cause slow re-inflation. The relatively large negative pressure of 9 kPa generated by the Ellicks bulb evaluator used in Dr Nunn's modification of the ODD may cause a 'suction effect' between the bevel of the tracheal tube and tracheal mucosa. Drs Williams and Nunn in their prospective clinical trial of 100 patients,[3] reported two cases of delayed refill from tracheal placed tubes. The advantage of using the syringe as a means of aspiration is that a constant slow aspiration can be achieved avoiding the 'suction effect'.[4]

I would, therefore, challenge Dr Baraka's conclusion that the ODD may fail to detect tracheal tube placement because of low lung compliance, as he has not presented any evidence to support this. On the contrary, it would seem that the ODD, when used correctly and when the clinician is aware of its limitations,[4] is particularly useful in cases of low lung compliance for the detection of tube placement. Last, but not least, it takes a few seconds to use the ODD and there is nothing to stop the clinician repeating the test after a 'twist and pull' manoeuvre[2,4] to confirm tracheal intubation in cases of doubt, without endangering patient safety.

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Cardiac arrhythmias during rigid oesophagoscopy

Rigid oesophagoscopy is a diagnostic procedure that may be associated with several complications including oesophageal perforation, aspiration pneumonia and cardiac arrhythmias. The latter occur most commonly as the oesophagoscope passes behind the heart and are generally regarded as being both transitory and of no real cause for concern.[1,2] We report the case of a patient who developed two serious arrhythmias during rigid oesophagoscopy performed under general anaesthesia.

The patient was a 74-year-old male weighing 64 kg with a potential diagnosis of oesophageal carcinoma. Pre-operatively he was well, taking no medication and full blood count, urea and electrolytes, blood sugar, chest X ray and electrocardiogram were all within normal limits. Premedication was with metoclopramide 10 mg and ranitidine 50 mg both given intramuscularly 90 minutes pre-operatively. On arrival in the operating theatre appropriate monitoring was commenced and fentanyl 50 μg given intravenously. This was followed by a rapid sequence induction consisting of 3 minutes pre-oxygenation, cricoid pressure, etomidate 14 mg, suxamethonium 75 mg and intubation with a cuffed size 8 mm orotracheal tube. Maintenance of anaesthesia was with nitrous oxide 66%, oxygen 33% and enflurane 0.6–1% and muscular paralysis provided by vecuronium 5 mg. During introduction of the oesophagoscope into the oesophagus the heart rhythm changed from a normal sinus rhythm of 68 beats/minute to rapid atrial fibrillation of 120–150 beats/minute. The oesophagoscope was immediately withdrawn and the atrial fibrillation reverted back to a normal sinus rhythm within one minute. A decision was made to re-introduce the oesophagoscope. This was promptly followed by ventricular tachycardia, which did not settle immediately the oesophagoscope was withdrawn. The patient's lungs were ventilated with 100% oxygen and cardiac massage commenced, followed by a 100 Joule DC shock, which restored sinus rhythm. A lignocaine infusion was started. The vecuronium was allowed to wear off spontaneously, the patient's trachea was extubated and he was sent to the coronary care unit for observation postoperatively.

This case demonstrates that cardiac arrhythmias occurring during rigid oesophagoscopy are not always transient and benign and can, in fact, be both prolonged and life threatening. Therefore it is mandatory that appropriate monitoring is applied to the patient before the procedure and that the anaesthetist is ready and able to deal promptly with any serious arrhythmia that may occur.

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Isoflurane anaesthesia in children

I read with some concern the suggestion by Professor Jones and his colleagues that 'in view of the uncertainty concerning the incidence of halothane hepatitis following repeated anaesthesia in children it is difficult to envisage circumstances in which halothane is clearly a superior agent' (*Anaesthesia* 1991; **46:** 686–8).

The authors found that isoflurane produced rapid and smooth induction of anaesthesia in unpremedicated children and, of course, their viewpoint must be respected. However, it has to be said that several studies have shown that airway irritation is more marked with isoflurane than with halothane.[1,2] It has been suggested that the production of secretions by isoflurane may make the airway more irritable,[3] a view supported by recent findings that the incidence and severity of airway complications is greater in the child who has not received pre-anaesthetic atropine.[4] Halothane has been widely used for gaseous induction of anaesthesia in children; its main advantage is that it causes minimal airway irritation. This is particularly important in the management of children with airway problems such as removal of a foreign body and acute epiglottitis. If coughing and larnygospasm become troublesome there is always the danger, especially in the infant, that control of the airway may be lost, a potentially dangerous situation if prior venous access has not been obtained.

It is, of course, of great concern that there have been isolated cases of halothane hepatitis in children, but the agent has had a remarkable record of safety when used for gaseous induction in paediatric practice. If it were discarded it would be unfortunate to find a higher incidence of other complications associated with the more widespread use of the presently available alternatives.

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Trimeprazine premedication in children

Like many other anaesthetists, I have used trimeprazine for paediatric premedication since its introduction in 1959. Apart from some children who dislike the taste, I have found it a satisfactory agent and I usually use it in a dose of 4 mg/kg, the dose previously recommended by the manufacturer to 'induce sleep'. A revised data sheet from the manufacturers now states: 'Pre-anaesthetic medication/ children 2–7 years. The *maximum* (my italics) dosage of Vallergan Forte syrup recommended for this indication is 2 mg/kg bodyweight'. I am unhappy at this new recommendation which seems to me effectively to deprive anaesthetists of a valuable sedative agent since, in the experience of myself, my colleagues and the ward sisters at my hospital, 2 mg/kg is frequently inadequate to sedate a frightened child and may often make matters worse.

On enquiry, the manufacturers quoted a single 10-year-old publication[1] suggesting that 2 mg/kg will be adequate as a premedicant. The data were based on children undergoing tonsillectomy. The conclusion of the authors was that either 2 mg/kg or 4 mg/kg was effective for premedication in children. No complications were reported with either dose. The manufacturers also drew attention to two reports of untoward occurrences following administration of trimeprazine.[2,3] However, the evidence of a simple dose-related relationship in the cases described is unconvincing.

It is particularly disturbing that the manufacturers have revised their data sheet without, as far as I know, formal consultation with the relevant professional organisations. I understand that doses in excess of 2 mg/kg are still widely used in paediatric centres throughout the country, and that at a recent meeting of the Association of Paediatric Anaesthetists of Great Britain and Ireland, a clear majority of those present indicated on a show of hands that they were continuing to use the drug at a dosage of 3 mg/kg.

Clearly the manufacturers need to protect themselves from recommending any drug dosage which is not compatible with safety. In the case of trimeprazine, however, the evidence on which the lower maximum drug dosage has been recommended seems to be very slender and both I and many others remain unconvinced that this is a sensible recommendation.

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A better extensometer

We report the laboratory testing of a new version of the extensometer or 'rubbery ruler.' According to the manufacturers the new extensometer can be stretched to 150% of its original length without being damaged (125% for the earlier version) and has an output that is more linearly related to elongation that the earlier version.[1]

The new extensometer is 250 mm in length and approximately 4 mm in diameter. It was stretched by 2.5 mm incremental lengths between 104% and 140% of its original length and the voltage output recorded. This was repeated 10 times by the same observer. The relationship between voltage output and length change over the stretch range 4–40% is shown in Figure 1. The R^2 value for this range was 0.981, there was no recordable error between any of the 10 testings, and the R^2 value for the stretch range 4–17% was 0.995. This compares to the value 0.987 obtained for the earlier RR over the same stretch range.[1] The R^2 value for the stretch range 17–40% was 0.998. Over the clinically useful stretch range the R^2 value approaches unity.

Laboratory testing of the new extensometer confirms that it is better than the original in that the output is more

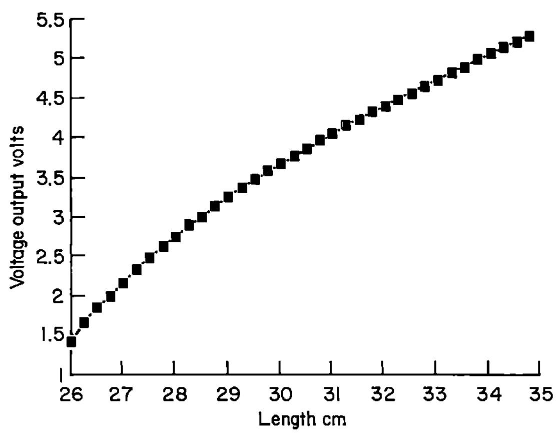

Fig. 1. Voltage output of the new extensometer plotted against elongation. $R^2 = 0.981$.

linear and it can be stretched further without being damaged. It is also softer and more pleasant to wear. The high linearity means that the extensometers applied to chest and abdomen only need to be stretched to approximately the same value to have identical outputs for a given change in circumference. This means that the new RR would be easier to apply and the output more accurate. It therefore has more potential in the field of respiratory pattern analysis than the original version.

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Research difficulties for junior anaesthetists

The difficulties experienced by Dr Akhtar in completing a research project (*Anaesthesia* 1991; **46:** 421) are common and, in many ways, a predictable problem for junior medical staff. The original editorial (*Anaesthesia* 1990; **45:** 909–10) correctly identified the relevant factors, 'the project must be well supervised and there must be sufficient time and resources to ensure it is completed'.

Good supervision should include a commitment to ensure the project is completed by recruiting another collaborator or by the supervisor taking on the remainder of the study when the junior staff member moves to another position. The Royal Perth hospital Ethics Committee now pays particular attention to the likelihood of a project being completed when protocols are submitted for approval. At least one of the investigators involved in any study must be a permanent member of the hospital's staff, who will assume responsibility for its completion. It is not ethical for people to be subjected to the stress and potential hazards or discomforts of participating in a study if it has to be stopped prematurely by predictable events such as the rotation of junior staff.

There are many useful lessons that can be learnt from participating in research projects. These include collaboration with others to ensure projects are completed and understanding the need to include sufficient patients to have a good chance of achieving a statistically significant result, a number which should be defined in the research protocol.

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Continued problems with diclofenac injections

We would like to report three cases of prolonged local reaction and abscess formation following intramuscular injection of diclofenac 75 mg ('Voltarol', Geigy). In all three patients the injection site was the thigh.

The first patient was a fit 33-year-old female who received an intra-operative injection of diclofenac 75 mg (3 ml) into the anterolateral aspect of her left thigh. Swelling and pain developed around the injection site after 3 days and she was re-admitted to hospital 10 days after discharge with a pyrexia of 38.5°C and a thigh abscess requiring incision and drainage; blood and pus cultures yielded no growth. The second patient was a fit 44-year-old female who received diclofenac 75 mg into her right thigh following laparoscopy. She initially reported bruising around the injection site and up to 4 months later an area of diffuse nodularity could be felt, which when X rayed had the appearance of early calcification. The nodularity has since resolved but the patient complained of a localised dull pain for 18 months until discharged from the outpatient department. The third patient was a fit 18-year-old male who received diclofenac 75 mg into the anterolateral aspect of his left thigh following insertion of a Denham pin. Twelve days later bruising and altered sensation were noted at the injection site and at 8 months review scarring of the thigh was still obvious (17 cm + 7 cm).

There have been two reports[1,2] describing swelling and skin necrosis at injection sites following intramuscular injection of diclofenac 75 mg, both of which were into the thigh. A review[3] of 10 167 cases of intramuscular diclofenac showed an incidence of six abscesses (0.05%) and three of necrosis (0.02%), although injection site was not specified. The data sheet provided with diclofenac recommends deep intragluteal injection but the *British National Formulary* does not specify any particular site for intramuscular injection.

In the light of the above reactions we have issued a hospital memorandum to all clinical departments emphasising that intramuscular diclofenac must be given by deep intragluteal injection only. Our hospital pharmacy has also issued labels, reiterating the same point, that are attached to each box of intramuscular diclofenac. The cases have been reported to the Committee on Safety of Medicines and we have also contacted Geigy Pharmaceuticals who have expressed concern and been most helpful. Intramuscular diclofenac is becoming a popular alternative or adjunct to opioid analgesia and thus we feel that it is important to emphasise that intramuscular diclofenac is given only by deep intragluteal injection, twice daily for a maximum of 2 days. We have found that diclofenac suppositories 100 mg can often be an effective alternative.

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Cardiorespiratory changes during upper gastrointestinal endoscopy

Drs Murray *et al* (*Anaesthesia* 1991; **46:** 181–4) rightly point out the marked physiological changes which can occur during endoscopy of the upper gastrointestinal tract, but their conclusion that pulse oximetry may be the most valuable monitor warrants comment. Whilst it is likely that ECG changes indicating myocardial ischaemia may be expected during periods of hypoxaemia, to extrapolate such a correlation from one patient is surely stretching the point.

The value of concomitant oxygen therapy should also be stressed. We have recently studied 52 patients (unpublished data) undergoing endoscopy. The first 16 patients became desaturated to < 90%, after which oxygen was administered at 4 litres/minute via nasal speculae to all patients. Subsequently no patient showed a saturation of less than 94%. This has been demonstrated by several other authors[1,2] and may have prevented ST segment changes, as reported by Dr Murray and colleagues. With regard to changes in blood pressure, we saw a much greater incidence of hypotension, 38 patients demonstrating a decrease in their systolic blood pressure of greater than 20% compared to their pre-endoscopy values. This, together with an increase in heart rate of more than 20% in 28 patients, confirms the potential for myocardial ischaemia and it is surprising that the ST segment changes in Dr Murray's study did not correlate with increases in rate pressure product.

The need for adequate monitoring as recommended by the Association of Anaesthetists of Great Britain and Ireland[3] is therefore clear and an automatic blood pressure recorder together with a pulse oximeter with a plethysmographic trace (rather than a simple signal strength indicator) may provide the necessary information. In patients with a history of ischaemic heart disease, continuous ECG monitoring is advisable together with the presence of a suitably qualified attendent who can interpret changes and respond accordingly.

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Safe use of propofol in a patient receiving tranylcypromine

We wish to report the safe use of propofol for induction of anaesthesia in a patient taking Parstelin twice daily (tranylcypromine 10 mg and trifluoperazine 1 mg). The patient was a 51-year-old, 56 kg female scheduled for block dissection of the right groin for malignant melanoma. She had had numerous general anaesthetics before, including during a course of electroconvulsive therapy 4 years previously. The most recent anaesthetic was for primary excision of a melanoma from the right ankle 21 months before. She had been taking Parstelin for 19 years, had continued taking the drug during her previous anaesthetics and was unwilling to consider stopping it on this occasion. Her other medication included propranolol 40 mg twice daily (for anxiety), diazepam 5 mg at night, temazepam 30 mg at night and Lomotil as required. Apart from the malignant disease and stable chronic anxiety/depression she was otherwise well.

Premedication was lorazepam 2 mg orally, 2 hours before surgery. Prior to induction of anaesthesia, the ECG was monitored continuously (heart rate 56 beats/minute) and the blood pressure measured at 1 minute intervals with a self-inflating arm cuff (110/60 mmHg). Anaesthesia was induced with propofol 160 mg and a laryngeal mask inserted. Maintenance was achieved with the patient breathing enflurane (1–2%) in nitrous oxide (67%) and oxygen (33%) from a Bain system. Small increments of fentanyl (total dose 75 μg) and morphine (total dose 5 mg) were given intravenously for analgesia.

The blood pressure fell to 70/37 mmHg after 3·minutes, rising again to 96/42 mmHg 3 minutes later. The heart rate reached 78 beats/minute maximum when the blood pressure was lowest and thereafter returned to 50-60 beats/minute. Both the heart rate and blood pressure were measured throughout the operation at two minute intervals (for 90 minute) and remained stable. Two litres of crystalloid were given during the procedure.

We report this case to confirm the observations of Powell,[1] especially as tranylcypromine is regarded as the most hazardous monoamineoxidase inhibitor (MAOI) because of its stimulant effects.[2] The only other report we can find of the safe use of propofol with MAOIs is that of Rouse[3] who successfully used propofol prior to electroconvulsive therapy in a patient taking isocarboxazid. It would appear propofol may be safely used in patients receiving MAOI treatment.

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Hazard with a triple lumen catheter

An 86-year-old woman was admitted to the Intensive Care Unit following open reduction and internal fixation of multiple long bone fractures sustained in a road traffic accident. A 20 cm Viggo Spectramed Secalon triple lumen Hydrocath central venous catheter (one 16 and two 18 gauge lumina) was inserted via the right subclavian vein by the lateral approach as part of her postoperative management. It was sutured in place at the skin entry point and at the hub and a chest X ray demonstrated a satisfactory position. Inotropes were infused through the 16 gauge lumen, total parenteral nutrition (TPN) through the first 18 gauge lumen, and the third lumen was used for central venous pressure measurement.

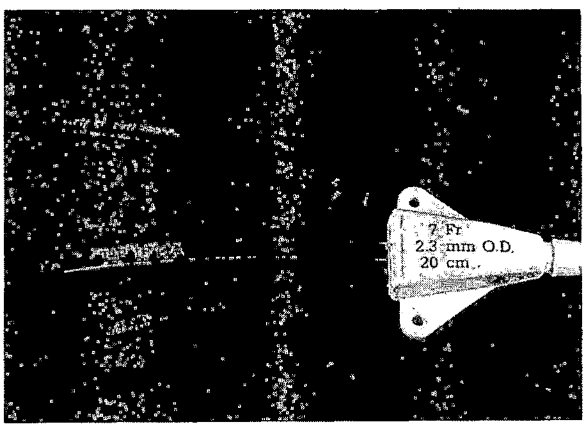

Fig. 1.

Forty-eight hours later, while the patient's lungs were still being ventilated and before any attempt had been made at weaning, one lumen was noted to be hanging loose. The patient end was immediately spigoted at the three-into-one hub from which it had become detached. The lumen involved was that dedicated to TPN via a volumetric pump at 40 ml per hour. The patient came to no harm and the catheter was promptly replaced. We are certain that no accidental stress had been put on this lumen and are unable to explain this event.

The catheter was returned to the manufacturer via the Department of Health Procurements Office. No fault was found with the remaining lumina, both of which exceeded the British Standard of 15 Newtons tension prior to disconnecting.

The procedure as detailed above is common in intensive care units and the authors are unaware of any previous reports on this problem. The disconnection of a central venous catheter renders the patient vulnerable to infection, haemorrhage and air embolism. The latter was prevented in this patient by a positive central venous pressure augmented by controlled ventilation and positive end expiratory pressure.

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A reply

Thank you for the opportunity to reply to the letter from Drs Walder and Tyler. As is mentioned in the letter, this incident was reported to the Department of Health and Viggo-Spectramed carried out a full investigation of the product, in line with our normal exhaustive procedures and in liaison with the Department of Health. These investigations failed to reveal any identifiable manufacturing defect.

We have experience of catheter fractures under stress, where the large number of lines in some patients has resulted in difficulties, either when turning the patient or moving equipment around the patient. There are also documented incidents involving over-pressure in infusion lines associated with infusion pumps. We remain unable to explain this incident in the absence of evidence of a manufacturing defect and if, as is suggested, no accidental stress was placed on the catheter.

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Percutaneous tracheostomy insertion can be difficult

I read with interest the recent paper by Bodenham *et al.* on percutaneous tracheostomy (*Anaesthesia* 1991; **46:** 570–2). The authors do not mention any difficulty in inserting the tracheostomy tube over the dilator. Both Ciaglia *et al.*[1] and Hazard *et al.*[2] comment on difficulty at this point in the procedure due to the tracheostomy tube catching on the tracheal cartilage as it is pushed over the dilator into the trachea. My own experience was obtained in Dunedin Public Hospital, New Zealand, where the 14-bedded Intensive Care Unit adopted percutaneous tracheostomy as routine in 1989. Both Shiley and Portex tubes were difficult to insert in more than half the patients, because the tip does not have the smooth taper of the dilators. In contrast, in all the patients, sequential dilatation to 36 FG had been easily achieved.

I thoroughly concur with the authors that a separate anaesthetist should be responsible for anaesthesia and analgesia for this painful procedure and in addition feel it is important, as with standard surgical tracheostomy, to ensure the tube lies within the trachea before removing the oral tube; in one patient a false tract was created.

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Resolution of acute brachial artery embolism following brachial plexus block

A 70-year-old woman presented for right brachial embolectomy. She had recently been admitted with an upper gastrointestinal haemorrhage which was treated conservatively. Shortly after admission she developed an anteroseptal myocardial infarct. She become increasingly dyspnoeic and despite treatment with diuretics and nitrates, required admission to the intensive care unit for ventilation. Pulmonary congestion secondary to poor left ventricular function was diagnosed. She remained stable except for occasional episodes of atrial fibrillation.

Five days after admission to the ICU, the patient was noted to have a cold, pale right forearm. Pulses distal to the axillary artery were absent and no flow was detectable by capillary refill, photoelectric plethysmography or Doppler ultrasound. In view of the recent myocardial infarct and episodes of atrial fibrillation, brachial embolism was diagnosed and the patient scheduled for embolectomy. Anaesthesia was provided by brachial plexus block, performed via the supraclavicular approach using 25 ml 0.375% bupivacaine. After 30 minutes the arm was hyperaemic and flow was detectable by Doppler ultrasound. Surgery was postponed and circulation in the right arm closely monitored. The patient was receiving low dose subcutaneous heparin and in view of the recent gastrointestinal haemorrhage, full anticoagulation was avoided. Digitalisation prevented further atrial fibrillation. At 18 hours pulses were present with a gradient of 30 mmHg between left and right arm systolic blood pressures. One week later, systolic blood pressures were equal in both arms.

Successful treatment of arterial embolus generally depends on early presentation, surgical restoration of normal circulation and anticoagulation.[1] Conservative management may be indicated in selected patients. This involves full heparinisation and use of thrombolytic agents.[2,3] Pratt reported using simultaneous sympathetic nerve blocks and anticoagulation in a large series of patients with varying vascular lesions,[4] but the use of sympathetic block in thromboembolism is not common practice.

Arterioles in the skin are normally under moderate alpha adrenergic vasoconstrictor influence and the principle circulatory effect of sympathetic blockade is an increased blood flow to the skin. Blood flow to muscle is largely regulated by local factors and depends on metabolic demand. The mechanisms by which flow was restored in this patient's arm is difficult to understand. The embolus may have been broken up by movement of the arm or massage of the ultrasound investigation. However, the timing suggests that the brachial plexus block played a significant part. A possible explanation is that the presence of an embolus in the brachial artery initiated a reflex resulting in local vasoospasm.[4] Sympathetic blockade interrupted this reflex resulting in increased flow via the brachial artery past the obstruction, allowing the action of intrinsic fibrinolytic mechanisms to break up the embolus. Early diagnosis and prompt attention may have played a part. Our experience with this case suggests that plexus or sympathetic block is worth considering in cases of peripheral arterial embolism. The patients most at risk are often on fibrinolytic or anticoagulation therapy and potential risks must be weighed against the potential benefits.

Royal Victoria Infirmary,
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C.H. Blumgart
B.Y.M. Ho

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Extradural vein puncture — an avoidable complication

I was interested to read the paper by Drs Mannion, Walker and Clayton (*Anaesthesia* 1991; **46:** 585–7) which found that the injection of 10 ml of normal saline in to the epidural space resulted in a significant reduction in the incidence of extradural vein cannulation. Bromage did not suggest the use of saline to distend the epidural space as stated by the authors of this paper. He in fact suggested that one third of the calculated main dose of local anaesthetic solution is injected directly up the needle,[1] i.e. 3 ml for a 10 ml main dose. I am also concerned that Dr Mannion and his colleagues do not say how much air in the syringe was used to locate the epidural space, or if this was controlled in the study. The amount of air in the syringe can have a bearing on the result as it has been shown that the injection of 10 ml of air, through the needle prior to epidural catheter insertion, reduces the incidence of extradural vessel puncture from 5.8 to 1.6%

Another recent study, using less than 2 ml of air in the syringe, found no reduction in the incidence of extradural vein trauma using either 3 ml of local anaesthetic or 3 ml of saline injected down the epidural needle.[3]

Manchester Royal Infirmary,
Oxford Road,
Manchester M13

B.J. Hendley

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Doxapram and shivering

I read with great interest the article by Sarma and Fry (*Anaesthesia* 1991; **46:** 460–1) concerning the effects of doxapram on shivering during recovery from anaesthesia and I would like to present the following comments.

It is well known for many years that thermogenesis and control of body temperature is very much dependent on the

level of oxygenation.[1] Shivering can be readily suppressed by hypoxia or after pharmacological stimulation of the arterial chemoreceptors.[2,3] As a consequence, it is not too surprising that a respiratory stimulant like doxapram will stop shivering in most patients recovering from anaesthesia.

Faculté de Médecine St Antoine, 75012 Paris, France H. GAUTIER

References

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Under pressure

Intravenous drug administration to patients in one-man hyperbaric oxygen chambers has posed a clinical problem since the inception of hyperbaric oxygen therapy. The difficulties are accentuated when patients are being artificially ventilated and require sedation and neuromuscular relaxants. During treatment patients may be isolated within the chamber for up to 3 hours, precluding the use of pre-administered bolus doses of sedatives and relaxants. The use of pressurized infusion systems controlled from outside the chamber has proved problematical, and clockwork syringe drivers unreliable.[1] Electrically powered devices are a fire risk in a pressurized, oxygen-enriched environment. We wish to report the Travenol Infusor,[2] Type 2C-10-73 5 ml/hour model, successfully delivers a constant rate infusion at ambient pressures up to 2.5 Atmospheres absolute.

A 25-year-old male patient was referred to this hospital for hyperbaric oxygen therapy following carbon monoxide poisoning. He was transferred with a tracheal tube *in situ* and his lungs were being ventilated. Two Travenol infusors, each delivering 5 ml/hour, were charged separately with midazolam 2 mg/ml and vecuronium 2 mg/ml, then connected intravenously in tandem. This provided adequate sedation and relaxation for the duration of therapy.

The flow delivered by the infusor is governed by the Poiseuille–Hagen formula, simplifed in practice to:

$$Q = k \times \frac{\triangle P}{\eta}$$

Q, volumetric flow rate; k, constant; $\triangle P$, differences in pressure between reservoir pressure (620 mmHg) and mean venous pressure; η, viscosity of fluid: dependent upon nature of fluid and inversely proportional to temperature.

The pressure difference remains constant across the fixed resistance of the rate controller in the device, as the pressure on both sides of the glass capillary are relative to ambient pressure. The elastomeric balloon drug reservoir must be carefully de-aired during filling. The drug solution viscosities for 5% dextrose (for which the device is calibrated), vecuronium 2 mg/ml and midazolam 2 mg/ml allow comparable flow through the infusor. Temperature was maintained constant by attaching both devices to the patient's skin and careful regulation of the chamber ambient temperature during pressurisation and depressurisation.

The Travenol infusor provides a reliable, safe and accurate technique for the administration of intravenous drug infusions in the isolated environment of the one-man hyperbaric oxygen chamber.

Princess Alexandra Hospital, Royal Air Force, Wroughton, Swindon SN4 0QJ

M.J. SPITTAL
J.P. WARWICK
S.J. HUNTER

References

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Obstructed ventilation: the blocked catheter mount

The lungs of a patient with Wegener's granulomatosis were being ventilated in the Intensive Care Unit because of deteriorating respiratory function precipitated by an atypical pneumonia. He was undergoing flexible bronchoscopy to obtain bronchial washings and bronchial alveolar fluid. The bronchoscope was passed through a rubber diaphragm on the tracheal tube connector and thus allowed ventilation to continue. During the procedure the oxygen saturation fell to approximately 80% and was slow to recover in spite of removing the bronchoscope and resealing the tracheal connector. At this point we decided to hand-ventilate the patient's lungs with 100% oxygen by using a Water's circuit connected to the tracheal tube by a catheter mount. However, it proved impossible to ventilate the lungs, the system being obstructed. It was felt that the system was blocked at the catheter mount since the Water's circuit had been checked before use and demonstrated no obstruction. The patient was disconnected from the catheter mount and the Water's circuit was connected directly to the tracheal tube via an angle-piece. It was then possible to ventilate the lungs.

On inspecting the catheter mount it was found that the lumen was totally occluded by a piece of black rubber. The black rubber was subsequently found to be the plug of the inflating tube to the cuff of a black anaesthetic facemask.

This catheter mount had just been taken from its sterile package immediately before use. It had been sent to the Intensive Care Unit from the Central Sterile Supply Department. Unfortunately, the patency of the catheter mount was not checked before its connection to the patient. This could easily have been done by either looking through the catheter mount or passing a bougie through its lumen to ensure free passage. The above illustrates how the unthinkable can happen with potentially disastrous results and why we should always check the patency of our connections.

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J. DUNNE
I. BALSON

Pre-operative removal of dentures

Three cheers for Drs Cobley's and Dunne's questioning of the old custom of removing a patient's dentures before coming to the operating theatre! (*Anaesthesia* 1991; **46:** 596). Seventeen years ago I raised the same question in a major general American medical journal and I invited comments.[1] I received a large number of letters from doctors in support of the idea.[2] Not only that, my little piece was picked up and abstracted by a national American women's weekly magazine and, as a result, I was deluged with letters from women from all over the U.S.A. praising my point of view!![3]

The volume of enthusiastic mail which I received from women of all ages was striking testimony that this seemingly minor matter can be of major emotional importance. Many patients have told me that the thing that they dread most about an operation is to be seen without their dentures. Indeed, many have told me that their husbands have never seen them without their teeth in place!

A little later, the matter was brought up in your columns by R.G. McGown[4] so I then wrote to tell you of my experience.[5] Now, after all these years, I can still confirm that it is good policy to allow patients to wear their dentures to the operating theatre.

For brief cases, one can use 'mask' anaesthesia with a nasal airway. When tracheal intubation is necessary one can leave the dentures in place for a short case. Often the lower denture comes a bit loose, and sometimes the upper one too if there is more than average pressure on the 'upper' by the laryngoscope. Even so, it is usually possible to complete the intubation process without difficulty. If the dentures come really loose, one just removes them. For longer cases it may be wise to remove the dentures at the last minute before 'induction'.

As for partial upper dentures, I believe that leaving them in place actually protects the remaining teeth from damage. The partial denture prevents the laryngoscope from slipping into the gaps which can hinder manipulation of the tube through the right side of the mouth. The presence of the 'partial' also lessens the chance of the laryngoscope prying apart the teeth which are adjacent to the gap.

Thus, I strongly support the position of Drs Cobley and Dunne. We should allow patients to wear their dentures to theatre, and often even when they 'go under' anaesthesia.

1393 Oak Avenue,
Los Altos,
California 94024, USA

D.V. THOMAS

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A co-axial technique for facilitating one-lung ventilation

A recent paper by Conacher (*Anaesthesia* 1991; **46:** 400–3) describes a co-axial technique for one lung ventilation. Reference is made to a communication from Nazari *et al*,[1] to whom priority for reporting this technique is described. I would like to point out that this method was first described by Dr Alberto Caputo in 1951.[2] Dr Caputo is now 74 years old, still working every day, mainly in the field of heart surgery. He is Director and Chairman of the Anesthetic Department of the Heart Institute Dante Pazzanese, a first class health complex that belongs to the São Paulo State Authority. He and his associates have helped to train more than 350 Brazilian anaesthetists and I believe that his work should also be recognized abroad.

It is my hope that you will publish this letter, so his research and effort will not be forgotten. It is a pity that the language barrier prevents Brazilian anaesthetists from being as widely known in Europe and the USA as they are in their own country.

Hospital Santo Antônio,
Santos,
SP Brazil CEP 11100

A. FORTUNA

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Erratum

Anaesthesia, 1991, Volume 46, page 792

Another antipollution device for the Jackson–Rees modification of Ayre's T-piece system

C.M. KUMAR

In the above letter, the name Ayre was incorrectly spelt when originally published. The correct version is presented here.

Anaesthesia, 1991, Volume 46, 1095–1146

Author Index, Volume 46 (1991)

c = correspondence; f = forum

Subject Index, Volume 46 (1991)

Keyword Index, Volume 46 (1991)

THE ASSOCIATION OF ANAESTHETISTS OF GREAT BRITAIN AND IRELAND

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......................19

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Dr M. Morgan, Department of Anaesthetics, Royal Postgraduate Medical School, Hammersmith Hospital, London W12 0HS, UK.

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Corporate author

The Committee on Enzymes of the Scandinavian Society for Clinical Chemistry and Clinical Physiology. Recommended method for the determination of gamma-glutamyltransferase in blood. *Scandinavian Journal of Clinical Laboratory Investigation* 1976; **36:** 119–25.

Anonymous. Epidemiology for primary health care. *International Journal of Epidemiology* 1976; **5:** 224–5.

BOOKS AND OTHER MONOGRAPHS

Personal author(s)

OSLER AG. Complement: mechanisms and functions. New York: Prentice-Hall, 1976.

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American Medical Association Department of Drugs. AMA drug evaluations, 3rd edn. New York: Publishing Sciences Group, 1977.

Editor, compiler, chairman as author

RHODES AJ, VAN ROOVEN CE, *comps. Textbook of virology: for students and practitioners of medicine and other health sciences*, 5th edn. Baltimore: The Williams & Wilkins Co., 1968.

Chapter in book

WEINSTEIN L. SWARTZ MN. Pathogenic properties of invading miro-organisms. In: SODEMAN WA Jr, SODEMAN WA, eds. *Pathologic physiology: mechanisms of disease.* Philadelphia: W.B. Saunders, 1974: 457–72

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National Center for Health Statistics. Acute conditions: incidence and associated disability, United States, July 1968—June 1969. Rockville, MD: National Center for Health Statistics, 1972. (*Vital and health statistics, Series* **10:** Data from the National Health Survey. No. 69) [DHEW publication No. (HSM) 72–1036].

OTHER ARTICLES

Newspaper article

SHAFFER RA. Advances in chemistry are starting to unlock mysteries of the brain: discoveries could help to cure alcoholism and insomnia, explain mental illness. How the messengers work. *Wall Street Journal* 1977 Aug 12: 1(col 1), 10(col 1).

Magazine article

ROUECHE B. Annals of medicine: the Santa Claus culture. *The New Yorker* 1971 Sept 4: 66–81.

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Anaesthesia

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